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TITLE: Drug Development and Conservation of Biodiversity in West and Central Africa/In Vitro Antiviral Screening of Plant Extracts and Isolates

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INTRODUCTION

This report outlines the antiviral evaluations for thirty-five (35) ICBG plant extracts For Walter Reed Army Institute of Research by Southern Research Institute.

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MATERIAL AND METHODS

Test Material

The thirty-five (35) plant extracts were received in vials containing 20 mg of dried powder. The extracts were solubilized in DMSO at 40 mg/mL and stored at -20° C until assay. No abnormal occurrences were noted upon solvation.

CEM-SS HIV-1_{RF} Cytoprotection Assay:

CEM-SS cells (obtained from the AIDS Research and Reference Reagent Repository, Bethesda, MD) are passaged in T-75 flasks in tissue culture media (RPMI 1640 medium (no phenol red) with 10% Fetal Bovine Serum (heat inactivated), 2 mM L-glutamine, 100 U/mL penicillin, 100 µg/mL streptomycin, and 10 µg/mL gentamycin). On the day preceding the assay, the cells are split 1:2 to assure they are in an exponential growth phase at time of infection. On the day of assay the cells are collected by centrifugation, washed twice with tissue culture medium and resuspended at 5 x 10⁴ cells per mL and resuspended in fresh tissue culture medium. Total cell and viability counting is performed using a hemacytometer. Cell viability prior to the assay is determined by Trypan Blue dye exclusion and must exceed 95%. A pretitered aliquot of HIV-1_{Rf} (AIDS Research and Reference Reagent Repository, Bethesda, MD), 5×10^3 cells and compound where appropriate are placed into 0.2 cm round bottom microtiter plates (final volume 200 µL). Each plate contains cell control wells (cells only), virus control wells (cells plus virus), drug toxicity control wells (cells plus drug only), drug colorimetric control wells (drug only) as well as experimental wells (drug plus cells plus virus) (Figure 1). Cultures are incubated for 6 days at 37°C, 5% CO₂ and antiviral activity and compound toxicity determined by MTS staining. Activity is confirmed by both macroscopic and microscopic analysis of the assay. Please note this assay was originally identified as the XTT

cytoprotection assay. The assays are identical except for the use of the MTS reagent in place of XTT for detection of cell viability.

Figure 1: Plate Layout for the HIV Cytoprotection Assay

	1	2	3	4	5	6	7	8	9	10	11	12
A	Media	Media	Media	Media	Media	Media	Blank	Blank	Blank	Blank	Blank	Blank
В	Cells +	Cell	(Cells + Virus		Cells +	Cells +	Cells + Virus			Cell	Cells +
	Drug 1	Control		+ Drug 1		Drug 1	Drug 2		+ Drug 2		Control	Drug 2
	0.32 μΜ		0.32 μΜ			0.32 μΜ	0.32 μΜ		0.32 μΜ			0.32 μΜ
C	Cells +	Cell	(Cells + Virus		Cells +	Cells +		Cells + Virus		Cell	Cells +
	Drug 1	Control		+ Drug 1		Drug 1	Drug 2		+ Drug 2		Control	Drug 2
	1 μM		1 μΜ			1 μM	1 μM		1 μΜ			1 μΜ
D	Cells +	Cell	Cells + Virus			Cells +	Cells +	Cells + Virus			Cell	Cells +
	Drug 1	Control		+ Drug 1		Drug 1	Drug 2	+ Drug 2			Control	Drug 2
	3.2 μΜ			3.2 μΜ		3.2 μM	3.2 μM		3.2 μΜ			3.2 μM
E	Cells +	Virus	(Cells + Virus		Cells +	Cells +	Cells + Virus			Virus	Cells +
	Drug 1	Control		+ Drug 1		Drug 1	Drug 2	+ Drug 2			Control	Drug 2
	10 μΜ			10 μM		10 μM	10 μM	10 μΜ				10 μM
F	Cells +	Virus	,	Cells + Virus		Cells +	Cells +		Cells + Virus	i	Virus	Cells +
	Drug 1	Control		+ Drug 1		Drug 1	Drug 2		+ Drug 2		Control	Drug 2
_	32 μM			32 μΜ		32 μM	32 μM		32 μM		37:	32 μM Cells +
G	Cells +	Virus	· '	Cells + Virus	•	Cells +	Cells +		Cells + Virus	5	Virus Control	1
	Drug 1	Control	+ Drug 1			Drug 1	Drug 2		+ Drug 2		Contion	Drug 2 100 μM
	100 μM		100 μΜ			100 μM	100 μM	Davis 2	100 μM	David 3	Drug 2	Drug 2
H	Drug 1	Drug 1	Drug 1	Drug 1	Drug 1	Drug 1	Drug 2	Drug 2	Drug 2	Drug 2	Drug 2	
	100 μΜ	32 μM	10 μM	3.2 μM	1 μM	0.32 μM	100 µM	32 μM	10 μM	3.2 µM + Media	1 μM + Media	0.32 μM + Media
	+ Media	+ Media	+ Media	+ Media	+ Media	+ Media	+ Media	+ Media	+ Media	→ Media	- Media	rivicuia

MTS staining for cell viability:

At assay termination the assay plates were stained with the soluble tetrazolium-based dye MTS (CellTiter Reagent Promega) to determined cell viability and quantify compound toxicity. MTS is metabolized by the mitochondria enzymes of metabolically active cells to a soluble formazan product, allowing the rapid quantitative analysis cell viability and compound cytotoxicity. This reagent is a single stable solution that does not require preparation before use. At termination of the assay 20 μ L of MTS reagent is added per well. The wells are incubated overnight for the HIV cytoprotection assay at 37°C. Adhesive plate sealers were used in place of the lids, the sealed plate was inverted several times to mix the soluble formazan product and the plate was read spectrophotometrically at 490 nm with a Molecular Devices Vmax plate reader.

Data Analysis:

Using an in-house computer program, IC $_{50}$ (50%, inhibition of virus replication), TC $_{50}$ (50% reduction in cell viability) and a therapeutic index (TI, TC $_{50}$ /IC $_{50}$) are provided. Raw data

for both antiviral activity and toxicity with a graphic representation of the data are provided in a printout summarizing the individual compound activity. We have provided AZT as a relevant positive control compounds for the individual assays.

RESULTS

The results of the antiviral evaluations for the compounds are summarized in **Table 1**. The raw data for each compound is included in **Appendix I** as a single page plate report. Antiviral data in the appendices for each test includes the relevant raw data values from the triplicate tests for virus replication and cell viability (OD 490) using MTS dye reduction. The IC_{50} and TC_{50} values are calculated by linear regression using a program developed specifically for this purpose at Southern Research Institute. The IC_{50} represents the compound concentration which suppresses virus replication by 50%, and the TC_{50} represents the compound concentration which results in 50% cytotoxicity. The TI represents the ratio of the TC_{50}/IC_{50} , and is used to determine relative potency between compounds. Compounds with a TI less than 2 are graded as inactive, 2<TI<5 are moderately active and TI>5 are active. The graphical representation shows the relationship between antiviral efficacy (%VC) and compound toxicity (%CC) expressed as a percent of the control, virus no compound or cells no compound, respectively.

It is important to note that initial antiviral evaluations of crude plant extracts rarely identify compounds with significant antiviral activity, since the antiviral moiety is usually a minor component of the total extract. In this case it is often helpful to use the IC_{25} (concentration inhibiting virus replication by 25%) to aid in identifying extracts with potentially active components. The relationship between the %VC and %CC curves can be further used to define extracts of interest.

The assays performed meet our internal validation and standardization criteria. For successful antiviral assays AZT must demonstrate an IC $_{50}$ between 1 and 10 nM without toxicity at the high test concentration of 4 μ M. The assays used to evaluate the plant extracts meet the individual assay standards and other internal assay validation criteria including intra-triplicate

variation and total virus replication. Thus, we consider the presented evaluations to be valid and representative of the antiviral activity of the tested extracts.

Table 1 summarizes the results of the testing of the 35 ICBG plant extracts in the HIV cytoprotection assay, and Table 2 summarizes compounds which reached and IC₂₅. Only compounds 1948 and 1961 demonstrated a TI greater than 2.0. Closer examination of the antiviral efficacy in both cases shows that antiviral activity is limited by compound toxicity, with complete protection prevented by increasing compound toxicity. Re-examination of the data using IC₂₅ values to identify plant extracts with potential antiviral activity yielded 6 more extracts which inhibited HIV replication sufficiently to produce an IC₂₅ (Table 2). Of the 6 extracts all extracts except 1960 have their antiviral activity limited by compound cyotoxicity. Although extract 1960 is non-toxic at 200 μ g/mL the abnormal shape of its antiviral efficacy curve raises doubts as to whether the observed protection is inhibition of virus replication or a cell-based effect and/or artifact. Extracts 1921 and 1959 are considered, based on the positioning of their antiviral efficacy and toxicity curves, to be the best lead compounds of the IC₂₅ group. Of the 35 extracts tested only extracts 1904, 1924, 1958, 1960 and 1965 were non-toxic to CEM-SS cells at the high test concentration of 200 μ g/mL.

DISCUSSION

We have analyzed thirty-five (35) ICBG plant extracts for anti-HIV activity in the HIV cytoprotection assay. This assay measures the ability of compounds to prevent the replication of the highly cytopathic Rf strain of HIV in the T-lymphoblastic cell line CEM-SS. Antiviral activity is evidenced by increased growth and viability of the cells following inhibition of virus replication. Two of the extracts (1948 and 1961) tested displayed antiviral activity which approached the level of marginal activity (2< TI<5) while 6 more of the extracts reached an IC₂₅. Further analysis of the extracts with IC₂₅s identified extracts 1921 and 1959 as the best lead extracts based upon the positioning of the antiviral efficacy and extract toxicity curves.

In general the extracts tested were cytotoxic to CEM-SS cells with extracts 1930 and 1914 being the most potent with TC_{50} s in the 1 μ g/ml range. Only 4 of the 35 extracts lacked any effect on

CEM-SS cell growth. Examination of the antiviral activity displayed by the four highlighted extracts (1948, 1961, 1921 and 1959) shows that for all four extracts cyotoxicity and antiviral activity were expressed in parallel. Thus these extracts will require further fractionation and/or purification to determine if antiviral activity is independent of cytotoxic constituents in the extracts.

TABLE 1 SUMMARY OF HIV CYTOPROTECTION RESULTS

Compound	IC ₅₀	TC ₅₀	Therapeutic
Сотронна	(µg/ml)	(μg/ml)	Index
AZT (μM)	0.004	>1.0	>250.0
1904	>200	200.0	
1909	>200	0.02	
1910	>200	121.0	
1911	>200	4.7	
1912	>200	77.2	
1914	>200	1.3	
1915	>200	12.8	
1916	>200	37.5	
1917	>200	38.7	
1918	>200	124.0	
1919	>200	39.4	
1920	>200	25.2	
1921	>200	42.2	
1923	>200	11.6	
1924	>200	>200	
1925	>200	42.4	
1927	>200	52.7	
1929	>200	0.003	
1930	>200	1.6	
1932	>200	101.0	
1933	>200	169.0	
1936	>200	60.9	
1946	>200	131.0	
1948	14.2	38.6	2.7
1953	>200	38.4	
1956	>200	123.0	
1957	>200	3.2	
1958	>200	>200	
1959	>200	44.4	
1960	>200	>200	
1961	17.6	45.3	2.6
1962	>200	41.5	

Compound	IC ₅₀ (μg/ml)	TC ₅₀ (μg/ml)	Therapeutic Index	
1963	>200	21.4		
1964	>200	4.5		
1965	>200	>200		

Table 2: Summary of Compounds Based on IC_{25} Values

Compound	IC ₂₅ (μg/ml)	TC ₂₅ (μg/ml)	Therapeutic Index
AZT (μM)	0.002	>1.0	>599.4
1921	17.7	25.9	1.5
1930	3.4	< 0.63	< 0.19
1932	53.4	52.6	0.98
1948	9.4	26.7	2.8
1959	5.0	1.9	0.38
1960	1.3	>200	>153.8
1961	10.3	32.6	3.2
1963	15.4	4.9	0.32

October 6, 2000

Submitted By:

Hm A. Turpin, Ph.D. Manager Retrovirus Research Laboratory Infectious Disease Research Department

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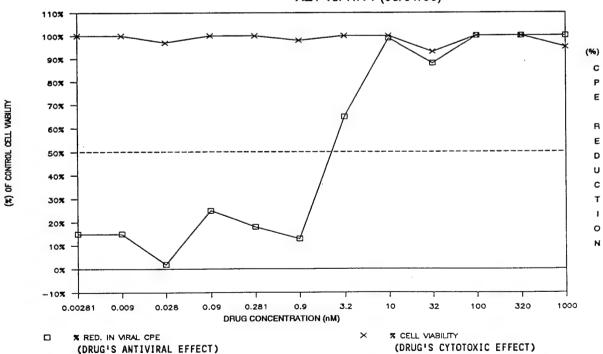
APPENDIX I HIV Cytoprotection Assay Results

VIRUS CELLS SHIPMENT NUMBER STRN	HIV1 CEMSS RF	PASSAGE PASSAGE OPERATOR 12S		PROJECT # SPONSOR TEST DATE DATE READ	 WALTERREED 08/01/00 08/01/00	
REAGENT	0.441	DRUG AZT	25%	50%	95%	
VIRUS CONTROL	0.268	TC (nM)	> 1.0000000	> 1.0000000	> 1.0000000	
CELL CONTROL	1.184	IC (nM)	0.0012100	0.0022200	0.0087500	
DIFFERENTIAL	0.916	ANTIVIRAL INDEX (AI)	> 829.1345220	> 450.5734920	> 114.3451240	

BOLD = highest drug conc

	DRUG AZT		ANTIVIRAL	TEST VALUES	CYTOTOXICITY	TEST VALUES		
	ROW ON	CONC.	MEAN	% RED. IN	MEAN	% CELL	COLORIMETRIC	
	PLATE	(nM)	O.D.	VIRAL CPE	O.D.	VIABILITY	- CONTROL	
BASED ON	low B	0.00281	0.135	15%	1.495	100%	0.006	
VALUES OF	С	0.009	0.135	15%	1.328	100%	0.006	
COLUMNS	D	0.028	0.021	2%	1.154	97%	005	
7 through 12	E	0.09	0.231	25%	1.228	100%	010	
(RIGHT SIDE	F	0.281	0.163	18%	1.283	100%	029	
OF PLATE)	G	0.9	0.119	13%	1.165	98%	003	
BASED ON	В	3.2	0.595	65%	1.257	100%	0.001	
VALUES OF	С	10	0.906	99%	1.236	100%	021	
COLUMNS	D	32	0.808	88%	1.106	93%	005	
1 through 6	E	100	1.030	100%	1.201	100%	0.025	
(LEFT SIDE	F	320	1.128	100%	1.278	100%	0.007	
OF PLATE)	high G	1000	0.999	100%	1.128	95%	0.039	

SUMMARY GRAPH --- AZT vs. HIV1 (08/01/00)



values shown are optical densities

tox=cell toxicity

cc=cell control

vc=virus control

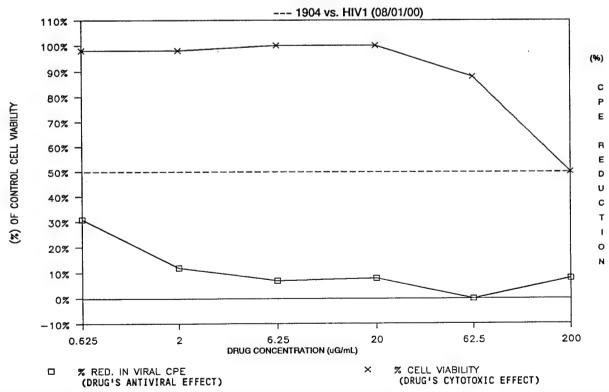
IN VITRO ANTIVIRAL RESULTS XTT ASSAY

DRUG: --- 1904 TAI: >7.44 SI: ---

	1	2	3	4	5	6	7	8	9	10	11	12
Г			reagent bac	kground					plastic backg	round		
Ä	0.412	0.407	0.427	0.426	0.418	0.451	0.054	0.058	0.056	0.059	0.061	0.063
ı	tox	cc/vc	dru	g 1904 exper	imental	tox					cc/vc	
В	1.615	1.646	1.395	0.735	0.810	1.661				l	1.542	
c	1.489	1.851	0.830	0.897	0.666	1.796					1.717	
Б	1.733	1.839	0.769	0.663	0.792	1.822					1.665	
E	1.740	0.744	0.924	0.641	0.656	1.759				ſ	0.739	
F	1.453	0.730	0.465	0.722	0.460	1.496					0.720	
G	0.805	0.721	1.101	0.604	0.435	1.142					0.701	
ı			colorimetric	background								
н	0.335	0.349	0.360	0.367	0.378	0.372						
	tov-cell to	ovicity co-	cell control	ve-virus co	ntrol	BOLD	m highest dru	ta couc		values sho	wn are optica	densities

VIRUS	HIV1	PASSAGE		PROJECT #	'
CELLS	CEMSS	PASSAGE		SPONSOR	WALTERREED
SHIPMENT NUMBER		OPERATOR KMW		TEST DATE	08/01/00
STRN	RF			DATE READ	08/01/00
REAGENT	0.424	DRUG 1904	25%	50%	95%
VIRUS CONTROL	0.302	TC (uG/mL)	110.00	200.00	> 200.00
CELL CONTROL	1.287	IC (uG/mL)	< 0.63		
DIFFERENTIAL	0.984	ANTIVIRAL INDEX (AI)	> 175.26		

DRUG 190	4	ANTIVIRAL	TEST VALUES	CYTOTOXICITY	TEST VALUES		
ROW ON	CONC.	MEAN	% RED. IN	MEAN	% CELL	COLORIMETRIC	
PLATE	(uG/mL)	O.D.	VIRAL CPE	O.D.	VIABILITY	CONTROL	
low B	0.625	0.305	31%	1.266	98%	051	
C	2	0.117	12%	1.264	98%	045	
D	6.25	0.072	7%	1.410	100%	056	
E	20	0.079	8%	1.390	100%	064	
F	62.5	102	0%	1.126	88%	075	
high G	200	0.076	8%	0.638	50%	088	



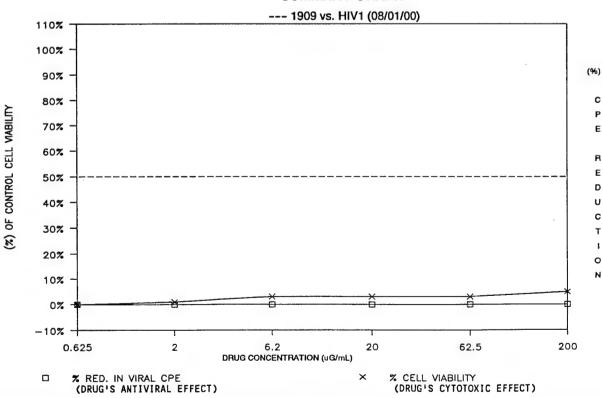
DRUG: --- 1909

TAI: 0.000000 SI: ----

	1	2	3	4	5	6	7	8	9	10	11	12
ſ			reagent back	ground					plastic backg	round		
A	0.412	0.407	0.427	0.426	0.418	0.451	0.054	0.058	0.056	0.059	0.061	0.063
1		cc/vc					tox	drug	1909 experi	mental	cc/vc	tox
В		1.646					0.398	0.399	0.402	0.430	1.542	0.437
С	}	1.851			1		0.440	0.420	0.436	0.439	1.717	0.418
Đ		1.839			Ì		0.520	0.503	0.517	0.504	1.665	0.544
E	Ī	0.744					0.656	0.652	0.660	0.641	0.739	0.693
F		0.730					0.905	0.888	0.914	0.842	0.720	0.916
G		0.721					1.144	1.178	1.184	1.110	0.701	1.191
1									colorimetric b	ackground		
H							1.097	0.877	0.629	0.494	0.422	0.447
	tox=cell toxicity cc=cell control vc=virus control BOLD = highest drug conc values shown are optical densities											

HIV1	PASSAGE		DDG 1505 #	
	INDONGE		PROJECT #	
CEMSS	PASSAGE		SPONSOR	WALTERREED
	OPERATOR KMW		TEST DATE	08/01/00
RF			DATE READ	08/01/00
0.424	DRUG 1909	25%	50%	95 %
0.302	TC (uG/mL)	< 0.63	< 0.63	200.00
1.287	IC (uG/mL)			
0.984	ANTIVIRAL INDEX (AI)			
	RF 0.424 0.302 1.287	RF 0.424 DRUG 1909 0.302 TC (uG/mL) 1.287 IC (uG/mL)	OPERATOR KMW RF 0.424 DRUG 1909 25% 0.302 TC (uG/mL) < 0.63 1.287 IC (uG/mL)	OPERATOR KMW TEST DATE RF DATE READ 0.424 DRUG 1909 25% 50% 0.302 TC (uG/mL) < 0.63 < 0.63 1.287 IC (uG/mL)

DRUG	190	9	ANTIVIRAL	TEST VALUES	CYTOTOXICITY	TEST VALUES			
ROW	ON	CONC.	MEAN	% RED. IN	MEAN	% CELL	COLORIMETRIC		
PLATE		(uG/mL)	O.D.	CPE	0.0.	VIABILITY	CONTROL		
low	В	0.625	340	0%	030	0%	0.024		
	С	2	292	0%	0.008	1%	002		
	D	6.2	289	0%	0.038	3%	0.071		
	E	20	281	0%	0.045	3%	0.206		
	F	62.5	299	0%	0.033	3%	0.454		
high	G	200	243	0%	0.070	5%	0.674		

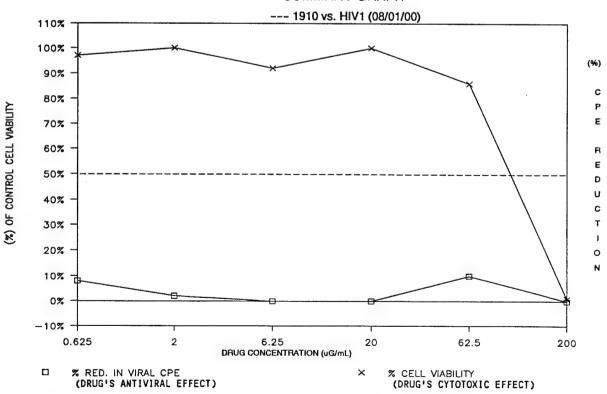


TAI: >0.75

	1	2	3	4	5	6	7	8	9	10	- 11	12
			reagent bac	kground					plastic backg	round		-
A	0.431	0.419	0.411	0.433	0.419	0.429	0.046	0.051	0.048	0.052	0.053	0.053
	tox	ec/vc	dru	2g 1910 exper	imental	tox				1	cc/vc	
В	1.714	1.775	0.788	0.852	0.960	1.761				1	1.733	
C	1.970	1.824	0.838	0.849	0.780	1.908					1.950	
D	1.788	1.749	0.740	0.746	0.731	1.634				I	1.740	
E	1.968	0.788	0.768	0.822	0.757	2.070				1	0.825	
F	1.803	0.770	1.133	1.232	1.082	1.918				İ	0.774	
G	1.093	0.880	1.061	1.075	1.037	1.007				1	0.714	
			colorimetric l	background								
Н	1.043	0.677	0.504	0.455	0.431	0.414						
	tox=cell to	oxicity cc=	cell control	vc=virus co	ntrol	BOLD	- highest dru	d conc		values sho	un are entire	Idensities

VIRUS CELLS SHIPMENT NUMBER STRN	HIV1 CEMSS RF	PASSAGE PASSAGE OPERATOR KMW		PROJECT # SPONSOR TEST DATE DATE READ	 WALTERREED 08/01/00 08/01/00
REAGENT	0.424	DRUG 1910	25%	50%	95%
VIRUS CONTROL	0.368	TC (uG/mL)	80.30	121.00	194.00
CELL CONTROL	1.372	IC (uG/mL)			
DIFFERENTIAL	1.003	ANTIVIRAL INDEX (AI)	****		

DRUG	191	0	ANTIVIRAL	TEST VALUES	CALOLOXICI	TY TEST VALUES	
ROW	ON	CONC.	MEAN	% RED. IN	MEAN	% CELL	COLORIMETRIC
PLA	TE (uG/mL)		O.D.	VIRAL CPE	O.D.	VIABILITY	CONTROL
LOW	В	0.625	0.085	8%	1.324	97%	010
	C	2	0.023	2%	1.508	100%	0.007
	D	6.25	084	0%	1.256	92%	0.031
	E	20	090	0%	1.515	100%	0.080
	F	62.5	0.104	10%	1.184	86%	0.253
nigh	G	200	353	0%	0.007	1%	0.619



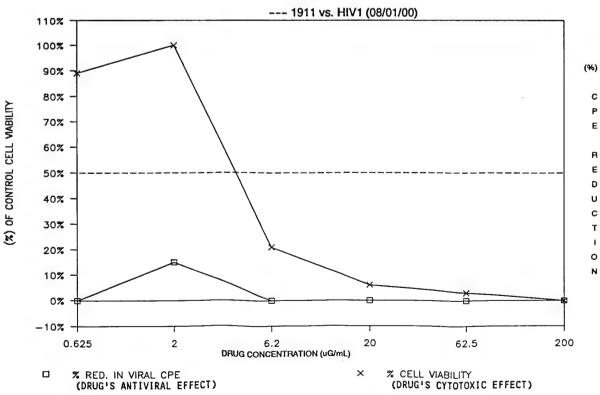
TAI: 1.11

DRUG: --- 1911 SI: ----

	1	2	3	4	5	6	7	8	9	10	. 11	12
Γ			reagent baci	ground		4			plastic backg	round		
A	0.431	0.419	0.411	0.433	0.419	0.429	0.046	0.051	0.048	0.052	0.053	0.053
ſ		cc/vc				3	tox	dru	g 1911 experi	mental	cc/vc	tox
8		1.775				1	1.730	0.744	0.758	0.822	1.733	1.643
C		1.824				į.	1.969	0.907	1.098	0.937	1.950	1.990
D		1.749			-		0.690	0.590	0.583	0.628	1.740	0.951
E		0.788				2.	0.673	0.649	0.611	0.648	0.825	0.663
F		0.770					1.051	1.009	0.955	0.954	0.774	0.962
G		0.880					1.371	1.335	1.333	1.321	0.714	1.147
1									colorimetric b	ackground		
н					_		1.347	0.966	0.582	0.535	0.464	0.462
•	tox=cell to	oxicity cc=	cell control	vc=virus co	ntrol	BOLD	- highest dru	g conc		values sho	own are optica	densities

VIRUS	HIV1	PASSAGE		PROJECT #	
CELLS	CEMSS	PASSAGE		SPONSOR	WALTERREED
SHIPMENT NUMBER	••	OPERATOR KMW		TEST DATE	08/01/00
STRN	RF			DATE READ	08/01/00
REAGENT	0.424	DRUG 1911	25 %	50%	95%
VIRUS CONTROL	0.368	TC (uG/mL)	3.34	4,69	34.20
CELL CONTROL	1.372	IC (uG/mL)		\$	
DIFFERENTIAL	1.003	ANTIVIRAL INDEX (AI)			

DRUG	191	1	ANTIVIRAL	L TEST VALUES CYTOTOXICITY		Y TEST VALUES	
ROW	ON	CONC.	MEAN	% RED. IN	MEAN	% CELL	COLORIMETRIC
PLATE		(uG/mL)	O.D.	CPE	O.D.	VIABILITY	CONTROL
low	В	0.625	055	0%	1.225	89%	0.038
	С	2	0.149	15%	1.516	100%	0.040
	D	6.2	303	0%	0.286	21%	0.111
	E	20	314	0%	0.086	6%	0.158
	F	62.5	361	0%	0.041	3%	0.542
high	G	200	385	0%	088	0%	0.923



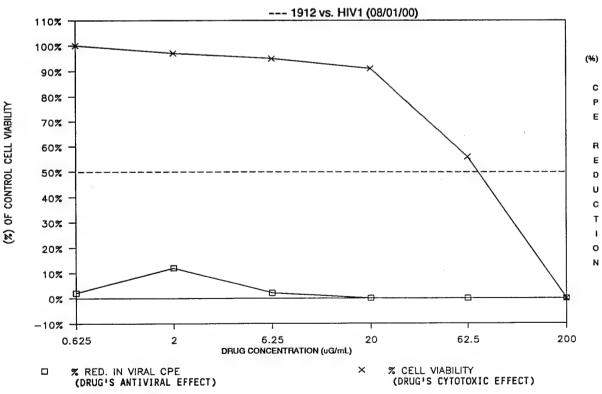
DRUG: --- 1912

TAI: >1.78 SI: ----

	1	2	3	4	5	6	7	8	9	10	11	12
ſ			reagent back	ground					plastic backg	round		
A	0.434	0.394	0.417	0.411	0.407	0.423	0.047	0.051	0.051	0.050	0.052	0.058
1	tox	oc/vc	dru	g 1912 exper	mental	tox					cc/vc	
В	1.895	1.827	0.689	0.735	0.790	1.720				1	1.585	
C	1.661	1.662	1.075	0.677	0.736	1.676					1.724	
D	1.649	1.718	0.908	0.711	0.611	1.668					1.703	
E	1.560	0.683	0.629	0.789	0.602	1.637					0.780	
F	1.139	0.648	0.588	0.885	0.626	1.200					0.622	
G	0.507	0.804	0.516	0.509	0.484	0.530					0.692	
1			colorimetric t	ackground								
Н	0.535	0.450	0.427	0.429	0.415	0.428						
•	tox=cell to	oxicity cc=	cell control	vc=virus co	ntrol	BOLD	- highest dru	ig conc		values sho	wn are optica	densities

VIRUS	,a _{e∈} HIV1	PASSAGE		PROJECT #	••
CELLS	CEMSS	PASSAGE		SPONSOR	WALTERREED
SHIPMENT NUMBER		OPERATOR KMW		TEST DATE	08/01/00
STRN	RF			DATE READ	08/01/00
REAGENT	0.414	DRUG 1912	25%	50%	95%
VIRUS CONTROL	0.291	TC (uG/mL)	39,40	77.20	188.00
CELL CONTROL	1.289	IC (uG/mL)			
DIFFERENTIAL	0.998	ANTIVIRAL INDEX (AI)			

DRUG 191	2	ANTIVIRAL	TEST VALUES	CYTOTOXICITY	TEST VALUES	
ROW ON	CONC.	MEAN	% RED. IN	MEAN	% CELL	COLORIMETRIC
PLATE	(uG/mL)	O.D.	VIRAL CPE	O.D.	VIABILITY	CONTROL
low B	0.625	0.019	2%	1.379	100%	0.014
C	2	0.123	12%	1.253	97%	0.001
D	6.25	0.023	2%	1.229	95%	0.015
E	20	045	0%	1.171	91%	0.013
E	62.5	041	0%	0.719	56%	0.036
high G	200	323	0%	017	0%	0.121



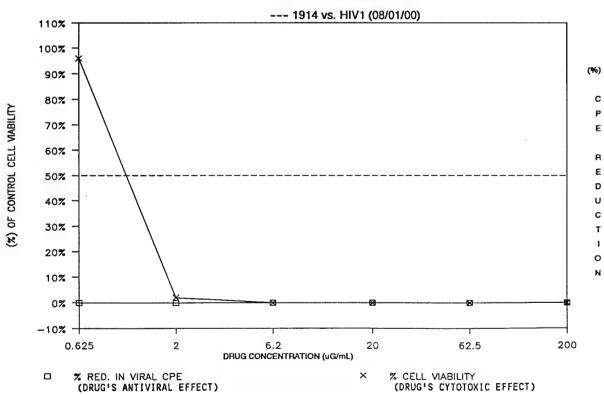
IN VITRO ANTIVIRAL RESULTS XTT ASSAY

DRUG: --- 1914 TAI: 0.000000 SI: ----

	1	2	3	4	5	6	7	8	9	10	11	12
Г			reagent back	ground					plastic backg	round		
A	0.434	0.394	0.417	0.411	0.407	0.423	0.047	0.051	0.051	0.050	0.052	0.058
- 1		cc/vc					tox	drug	g 1914 experi	mental	cc/vc	tox
В		1.827					1.728	0.679	0.685	0.713	1.585	1.660
C		1.662			ļ		0.441	0.382	0.383	0.399	1.724	0.469
D		1.718			ļ		0.399	0.383	0.397	0.405	1.703	0.429
E	ſ	0.683					0.397	0.393	0.391	0.414	0.780	0.433
F		0.648					0.377	0.372	0.383	0.392	0.622	0.418
G		0.804					0.390	0.390	0.400	0.404	0.692	0.425
Г								(colorimetric b	ackground		
Н							0.402	0.428	0.414	0.421	0.430	0.454
_	tox=cell toxicity cc=cell control vc=virus control BOLD = highest drug conc values shown are optical densities											

VIRUS	HIV1	PASSAGE		PROJECT #	
CELLS	CEMSS	PASSAGE		SPONSOR	WALTERREED
SHIPMENT NUMBER		OPERATOR KMW		TEST DATE	08/01/00
STRN	RF			DATE READ	08/01/00
REAGENT	0.414	DRUG 1914	25%	50%	95 %
VIRUS CONTROL	0.291	TC (uG/mL)	0.93	1.30	1.96
CELL CONTROL	1.289	IC (uG/mL)			
DIFFERENTIAL	0.998	ANTIVIRAL INDEX (AI)			

DRUG 191	4	ANTIVIRAL	TEST VALUES	CYTOTOXICITY	TEST VALUES	
ROW ON	CONC.	MEAN	% RED. IN	MEAN	% CELL	COLORIMETRIC
PLATE	(uG/mL)	O.D.	CPE	O.D.	VIABILITY	CONTROL
LOW B	0.625	053	0%	1.240	96%	0.040
C	2	333	0%	0.025	2%	0.016
D	6.2	317	0%	007	0%	0.007
Ε	20	306	0%	0.001	0%	0.000
F	62.5	337	0%	031	0%	0.014
high G	200	295	0%	0.005	0%	012

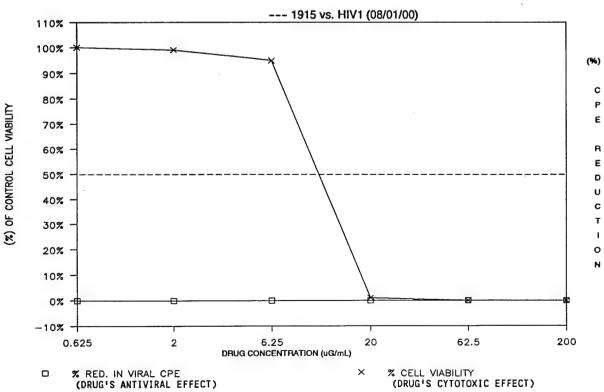


DRUG: --- 1915 TAI: 0.000000 SI: ----

	1	2	3	4	5	6	7	8	9	10	11	12
- 1			reagent bac	kground			plastic background					
A	0.386	0.387	0.384	0.377	0.382	0.413	0.054	0.056	0.055	0.056	0.058	0.062
- 1	tox	ec/vc	dru	g 1915 experi	mental	tox					cc/vc	
В	1.540	1.535	0.697	0.686	0.626	1.676				1	1.620	
C	1.557	1.554	0.593	0.685	0.753	1.611				ı	1.549	
D	1.488	1.607	0.544	0.609	0.550	1.619					1.593	
E	0.469	0.724	0.423	0.487	0.426	0.447	1				0.709	
F	0.510	0.641	0.494	0.464	0.504	0.508					0.690	·
G	0.769	0.682	0.788	0.776	0.707	0.675					0.635	
			colorimetric t	ackground								
н	0.758	0.523	0.450	0.423	0.407	0.418						
	tox=cell to	xicity cc-	cell control	vc=virus cor	ntrol	BOLD	= highest dru	g conc		values sho	wn are optica	l densities

VIRUS CELLS SHIPMENT NUMBER STRN	HIV1 CEMSS RF	PASSAGE PASSAGE OPERATOR KMW		PROJECT # SPONSOR TEST DATE DATE READ	 WALTERREED 08/01/00 08/01/00
REAGENT	0.388	DRUG 1915	25%	50%	95%
VIRUS CONTROL	0.292	TC (uG/mL)	9.18	12.80	19_40
CELL CONTROL	1.188	IC (uG/mL)			
DIFFERENTIAL	0.896	ANTIVIRAL INDEX (AI)			

DRUG 19	15	ANTIVIRAL	TEST VALUES	CYTOTOXICITY	TEST VALUES	
ROW ON	CONC.	MEAN	% RED. IN	MEAN	% CELL	COLORIMETRIC
PLATE	(uG/mL)	O.D.	VIRAL CPE	0.0.	VIABILITY	CONTROL
LOW B	0.625	040	0%	1.190	100%	0.030
C	2	022	0%	1.177	99%	0.019
D	6.25	147	0%	1.130	95%	0.035
E	20	297	0%	0.008	1%	0.062
F	62.5	328	0%	014	0%	0.135
high G	200	293	0%	036	0%	0.370



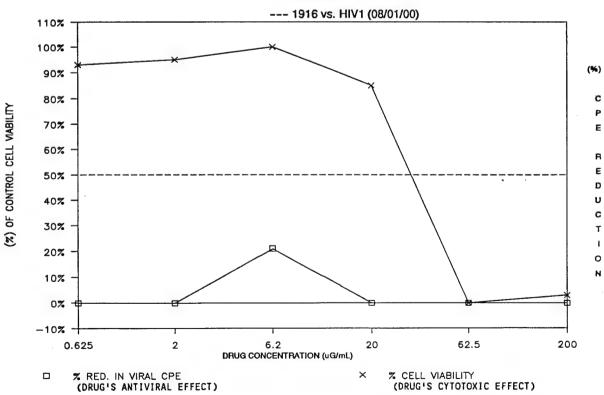
DRUG: --- 1916 TAI: 2.91

SI: -

	1	2	3	4	5	6	7	8	9	10	11	12
Γ			reagent back	ground					plastic backg	round		
A	0.386	0.387	0.384	0.377	0.382	0.413	0.054	0.056	0.055	0.056	0.058	0.062
Ī		oc/vc					tox	dru	1916 experi	mental	cc/vc	tox
В	j	1.535					1.558	0.630	0.750	0.720	1.620	1.541
C		1.554					1.535	0.660	0.602	0.695	1.549	1.562
D		1.607					1.619	1.550	0.585	0.610	1.593	1.645
Ε		0.724					1.245	0.580	0.633	0.556	0.709	1.658
F		0.641					0.495	0.474	0.462	0.471	0.690	0.505
G		0.682					0.662	0.633	0.614	0.618	0.635	0.628
- 1									colorimetric b	ackground		
н							0.614	0.497	0.442	0.435	0.416	0.448
•	day and de		sell control	No-virue cor	trol	DOLD.	- highest dru			velues she	wa are entire	t danateina

VIRUS CELLS SHIPMENT NUMBER	••	PASSAGE PASSAGE OPERATOR KMW		PROJECT # SPONSOR TEST DATE	WALTERREED 08/01/00
STRN	RF			DATE READ	08/01/00
REAGENT	0.388	DRUG 1916	25%	50%	95 %
VIRUS CONTROL	0.292	TC (uG/mL)	25.00	37.50	60.00
CELL CONTROL	1.188	IC (uG/mL)			
DIFFERENTIAL	0.896	ANTIVIRAL INDEX (AI)			

DRUG 1	916		ANTIVIRAL	TEST VALUES	CYTOTOXICITY	TEST VALUES	
ROW C	N C	ONC.	MEAN	% RED. IN	MEAN	% CELL	COLORIMETRIC
PLAT	E (uG	/mL)	O.D.	CPE	O.D.	VIABILITY	CONTROL
low B	0.	625	040	0%	1.101	93%	0.060
C		2	056	0%	1.132	95%	0.028
D		6.2	0.188	21%	1.197	100%	0.047
E		20	144	0%	1.009	85%	0.054
F	6	2.5	320	0%	0.003	0%	0.109
high G	:	200	285	0%	0.031	3%	0.226



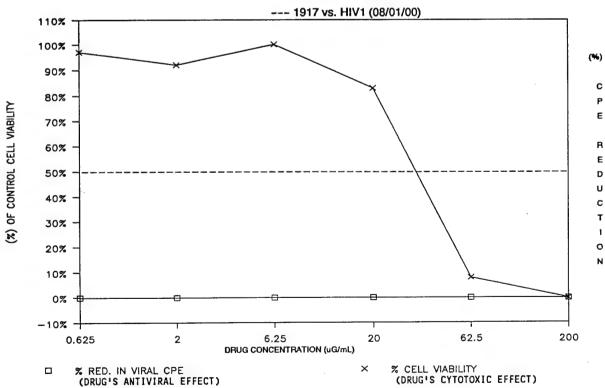
IN VITRO ANTIVIRAL RESULTS XTT ASSAY

DRUG: --- 1917 TAI: 0.000000 SI: -----

	1	2	3	4	5	6	7	8	9	10	11	12
ſ			reagent back	ground					plastic backg	round		
A	0.419	0.345	0.390	0.390	0.393	0.404	0.063	0.068	0.068	0.069	0.071	0.071
- 1	tox	oc/vc	dru	g 1917 exper	mental	tox					cc/vc	
В	1.468	1.512	0.633	0.758	0.748	1.654					1.581	
c	1.410	1.530	0.611	0.657	0.699	1.599					1.577	
D	1.512	1.564	0.601	0.622	0.675	1.703					1.651	
E	1.245	1.113	0.521	0.511	0.565	1.481					0.684	
F	0.475	0.816	0.494	0.490	0.515	0.533				ĺ	0.810	
G	0.438	0.711	0.415	0.417	0.394	0.428					0.775	
- 1			colorimetric b	ackground								
н	0.433	0.409	0.388	0.411	0.417	0.420						
٠,	tav. salt te	violet on	eell control	Vo-virue co	ntroi	BO! D	- bigbest dru	IC CODC		values sho	wn are ontica	I densities

VIRUS CELLS SHIPMENT NUMBER STRN	HIV1 CEMSS RF	PASSAGE PASSAGE OPERATOR KMW		PROJECT # SPONSOR TEST DATE DATE READ	 WALTERREED 08/01/00 08/01/00
REAGENT	0.390	DRUG 1917	25%	50%	95%
VIRUS CONTROL	0.428	TC (uG/mL)	24.50	38.70	114.00
CELL CONTROL	1.179	IC (uG/mL)			
DIFFERENTIAL	0.751	ANTIVIRAL INDEX (AI)			

DRUG 191	7	ANTIVIRAL	TEST VALUES	CYTOTOXICIT	Y TEST VALUES	
ROW ON	CONC.	MEAN	% RED. IN	MEAN	% CELL	COLORIMETRIC
PLATE	(uG/mL)	O.D.	VIRAL CPE	O.D.	VIABILITY	CONTROL
LOW B	0.625	135	0%	1.141	97%	0.030
С	2	190	0%	1.087	92%	0.027
D	6.25	207	0%	1.196	100%	0.021
E	20	284	0%	0.975	83%	002
F	62.5	338	0%	0.095	8%	0.019
high G	200	453	0%	0.000	0%	0.043



DRUG: --- 1918

TAI: 5.49

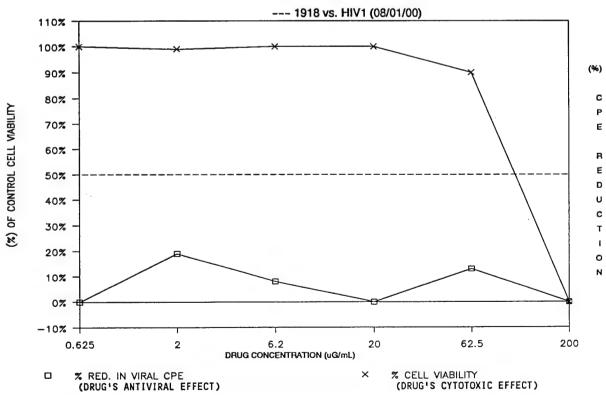
SI:	

	1	2	3	4	5	6	7	8	9	10	11	12
Г			reagent back	ground					plastic backg	round		
A	0.419	0.345	0.390	0.390	0.393	0.404	0.063	0.068	0.068	0.069	0.071	0.071
1		oc/vc					tox	dru	g 1918 experi	imentai	cc/vc	tox
В		1.512					1.667	0.688	0.713	0.698	1.581	1.651
С		1.530					1.507	0.732	0.735	1.513	1.577	1.660
D		1.564					1.800	1.016	1.061	0.737	1.651	1.609
E		1.113					1.831	0.893	0.902	0.795	0.684	1.733
F		0.816					1.716	1.477	0.985	1.097	0.810	1.720
G	1	0.711					0.968	0.945	0.959	0.935	0.775	0.964
- 1									colorimetric b	ackground		
н							1.010	0.661	0.494	0.450	0.419	0.448
•	tox=cell to	oxicity cc=	cell control	vc=virus cor	ntrol	BOLD	= highest dru	g conc		values sho	wn are optica	l densities

VIRUS CELLS SHIPMENT NUMBER	HIV1 CEMSS RF	PASSAGE PASSAGE OPERATOR KMW
STRN	Kr	
REAGENT	0.390	DRUG 1918
VIRUS CONTROL	0.428	TC (uG/mL)
CELL CONTROL	1.179	IC (uG/mL)
DIFFERENTIAL	0.751	ANTIVIRAL INDEX (AI)

	PASSAGE		PROJE	ECT #		
SS	PASSAGE		SPONS	SOR	WALTERREED	
	OPERATOR KMW		TEST	DATE	08/01/00	
			DATE	READ	08/01/00	
0	DRUG 1918	25%		50 %	95%	
3	TC (uG/mL)	85.40		124.00	192.00	
9	IC (uG/mL)					

						-
DRUG 19	18	ANTIVIRAL	TEST VALUES	CYTOTOXICITY	TEST VALUES	
ROW ON	CONC.	MEAN	% RED. IN	MEAN	% CELL	COLORIMETRIC
PLATE	(uG/mL)	O.D.	CPE	O.D.	VIABILITY	CONTROL
low B	0.625	177	0%	1.211	100%	0.058
C	2	0.146	19%	1.164	99%	0.029
D	6.2	0.060	8%	1.254	100%	0.060
E	20	059	0%	1.288	100%	0.104
F	62.5	0.097	13%	1.057	90%	0.271
nigh G	200	492	0%	044	0%	0.620

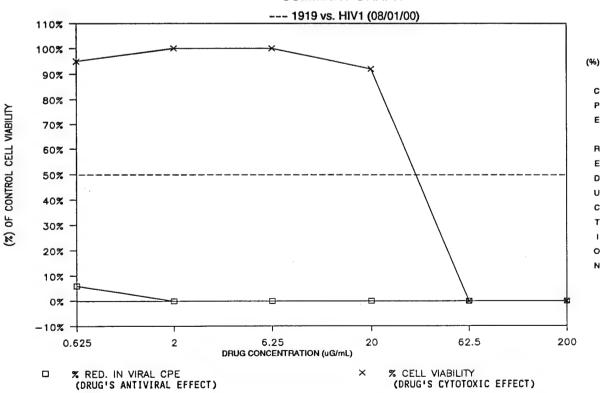


DRUG: --- 1919 SI: ---TAI: >0.10

	1	2	3	4	5	6	7	8	9	10	11	12
ſ			reagent back	ground					plastic backg	round		
A	0.405	0.361	0.378	0.373	0.379	0.373	0.045	0.050	0.049	0.055	0.055	0.061
1	tox	oc/vc	dru	g 1919 experi	mental	tox					cc/vc	
В	1.556	1.524	0.791	1.035	0.770	1.645				i	1.661	
C	1.870	1.625	1.004	0.725	0.630	1.855					1.593	
D	1.608	1.604	0.692	0.656	0.724	1.836					1.631	
E	1.419	1.132	0.629	0.652	0.591	1.690					0.650	
F	0.449	0.714	0.424	0.433	0.428	0.408					0.700	·
G	0.458	0.710	0.448	0.464	0.472	0.466					0.655	
- [colorimetric b	ackground								
н	0.477	0.428	0.423	0.416	0.434	0.429						
•	tox=cell to	tox=cell toxicity cc=cell control vc=virus control					= highest dru	g conc		values sho	wn are optica	l densities

VIRUS CELLS SHIPMENT NUMBER	••	PASSAGE PASSAGE OPERATOR KMW	PROJECT # SPONSOR TEST DATE DATE READ	 WALTERREED 08/01/00 08/01/00	
STRN REAGENT	RF 0.378	DRUG 1919	25%	50%	95%
VIRUS CONTROL	0.382	TC (uG/mL)	27.90	39.40	60.20
CELL CONTROL	1.228	IC (uG/mL)			
DIFFERENTIAL	0.846	ANTIVIRAL INDEX (AI)			

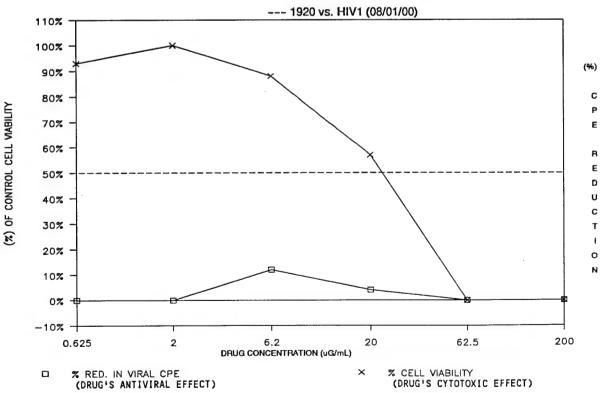
DRUG 191	9	ANTIVIRAL	TEST VALUES	CYTOTOXICITY		
ROW ON	CONC.	MEAN	% RED. IN	MEAN	% CELL	COLORIMETRIC
PLATE	(uG/mL)	O.D.	VIRAL CPE	O.D.	VIABILITY	CONTROL
low B	0.625	0.054	6%	1.171	95%	0.051
С	2	030	0%	1.428	100%	0.056
D	6.25	107	0%	1.306	100%	0.038
E	20	181	0%	1.131	92%	0.045
F	62.5	382	0%	0.000	0%	0.050
high G	200	398	0%	015	0%	0.099



	1	2	3	4	5	6	7	8	9	10	11	12
Г			reagent back	ground					plastic backg	round	÷	
	0.405	0.361	0.378	0.373	0.379	0.373	0.045	0.050	0.049	0.055	0.055	0.0
r		cc/vc					tox	dru	g 1920 experi	mental	cc/vc	tox
П		1.524					1.544	0.793	0.762	0.840	1.661	1.59
:	i	1.625					1.746	0.615	0.685	0.747	1.593	1.5
		1.604					1.544	0.770	0.629	1.334	1.631	1.4
1	İ	1.132					1.158	0.625	0.621	1.375	0.650	1.1
ı		0.714			-		0.506	0.563	0.620	0.570	0.700	0.5
١		0.710					0.670	0.668	0.618	0.647	0.655	0.6
h									colorimetric b	ackground		
١							0.696	0.516	0.457	0.430	0.418	0.4

VIRUS CELLS SHIPMENT NUMBER STRN	HIV1 CEMSS RF	PASSAGE PASSAGE OPERATOR KMW		PROJECT # SPONSOR TEST DATE DATE READ	 WALTERREED 08/01/00 08/01/00
REAGENT	0.378	DRUG 1920	25%	50%	95 %
VIRUS CONTROL	0.382	TC (uG/mL)	12.00	25.20	58.80
CELL CONTROL	1.228	IC (uG/mL)			•
DIFFERENTIAL	0.846	ANTIVIRAL INDEX (AI)			

DRUG 192	0	ANTIVIRAL	TEST VALUES	CYTOTOXICITY	TEST VALUES	
ROW ON	CONC.	MEAN	% RED. IN	MEAN	% CELL	COLORIMETRIC
PLATE	(uG/mL)	O.D.	CPE	O.D.	VIABILITY	CONTROL
low B	0.625	009	0%	1.145	93%	0.047
С	2	118	0%	1.224	100%	. 0.040
D	6.2	0.099	12%	1.079	88%	0.052
E	20	0.034	4%	0.696	57%	0.079
F	62.5	314	0%	003	0%	0.138
high G	200	434	0%	031	0%	0.318



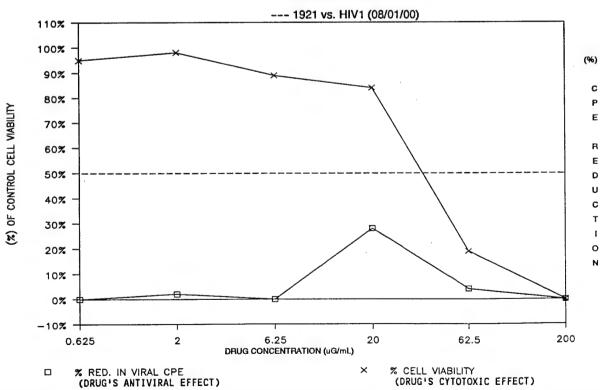
TAI: 0.79

DRUG: --- 1921 .79 SI: ----

	1	2	3	4	5	6	7	8	9	10	11	12
Г			reagent back	kground					plastic backg	round		
A	0.381	0.366	0.370	0.361	0.369	0.363	0.046	0.044	0.044	0.053	0.055	0.053
Ì	tox	ec/vc	dru	g 1921 experi	imental	tox					cc/vc	
В	1.436	1.574	0.627	0.647	0.613	1.572					1.489	
c	1.453	1.633	0.659	0.637	0.623	1.577				•	1.662	
D	1.379	1.486	0.589	0.656	0.601	1.463					1.606	
E	1.457	0.681	0.704	1.229	1.061	1.460					0.664	
F	0.508	0.675	0.534	0.867	0.933	0.865					0.626	
G	0.469	0.687	0.487	0.470	0.492	0.481					0.645	
1			colorimetric b	ackground								
н	0.500	0.451	0.448	0.352	0.327	0.357						
•	tox=cell to	tox=cell toxicity cc=cell control vc=virus control					- highest dru	g conc		values sho	wn are optica	i densities

VIRUS CELLS SHIPMENT NUMBER STRN	HIV1 CEMSS RF	PASSAGE PASSAGE OPERATOR KMW		PROJECT # SPONSOR TEST DATE DATE READ	 WALTERREED 08/01/00 08/01/00
REAGENT	0.368	DRUG 1921	25%	50 %	95%
VIRUS CONTROL	0.295	TC (uG/mL)	25.90	42.20	164.00
CELL CONTROL	1.207	IC (uG/mL)	17.70		
DIFFERENTIAL	0.912	ANTIVIRAL INDEX (AI)	1.47		

DRUG 192	1	ANTIVIRAL	TEST VALUES	CYTOTOXICIT		
ROW ON CONC		MEAN	% RED. IN	MEAN	% CELL	COLORIMETRIC
PLATE	(uG/mL)	O.D.	VIRAL CPE	0.0.	VIABILITY	CONTROL
low B	0.625	023	0%	1.147	95%	011
С	2	0.018	2%	1.188	98%	041
D	6.25	032	0%	1.069	89%	016
E	20	0.255	28%	1.010	84%	0.080
F	62.5	0.032	4%	0.235	19%	0.083
high G	200	312	0%	025	0%	0.132

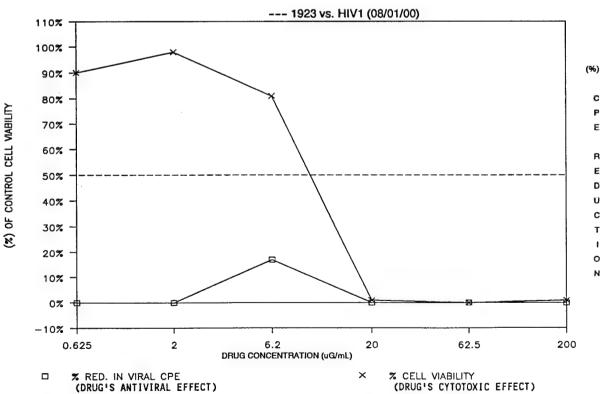


DRUG: --- 1923 TAI: 0.000000 SI: ----

	1	2	3	4	5	6	7	8	9	10	11	12
Г			reagent back	ground					plastic backg	round		
١l	0.381	0.366	0.370	0.361	0.369	0.363	0.046	0.044	0.044	0.053	0.055	0.053
٢		ec/ve					tox	dru	g 1923 experi	mental	cc/vc	tox
	1	1.574					1.538	0.586	0.598	0.578	1.489	1.540
		1.633					1.618	0.689	0.872	0.511	1.662	1.601
		1.486					1.417	0.932	0.484	1.184	1.606	1.379
	Ī	0.681					0.499	0.430	0.459	0.448	0.664	0.471
ı		0.675					0.539	0.529	0.509	0.521	0.626	0.540
		0.687					0.717	0.725	0.693	0.708	0.645	0.750
1									colorimetric b	ackground		
1							0.726	0.568	0.472	0.415	0.431	0.451
_	tox=cell to	xicity cc-	cell control	vc=virus co	ntroi	BOLD	= highest dru	ig conc		values sho	wn are optica	densities

HIV1	PASSAGE		PROJECT #	
CEMSS	PASSAGE		SPONSOR	WALTERREED
	OPERATOR KMW		TEST DATE	08/01/00
RF			DATE READ	08/01/00
0.368	DRUG 1923	25%	50%	95 X
0.295	TC (uG/mL)	7.28	11.60	19.30
1.207	IC (uG/mL)			
0.912	ANTIVIRAL INDEX (AI)			
	CEMSS RF 0.368 0.295 1.207	CEMSS PASSAGE OPERATOR KMW RF 0.368 DRUG 1923 0.295 TC (UG/mL) 1.207 IC (UG/mL)	CEMSS PASSAGE OPERATOR KMW RF 0.368 DRUG 1923 25% 0.295 TC (uG/mL) 7.28 1.207 IC (uG/mL)	CEMSS PASSAGE OPERATOR KMW SPONSOR TEST DATE DATE DATE READ 0.368 DRUG 1923 25% 50% 0.295 TC (uG/mL) 7.28 11.60 1.207 IC (uG/mL)

DRUG 19	23	ANTIVIRAL TEST VALUES		CYTOTOXICITY	TEST VALUES	
ROW ON	CONC.	MEAN	% RED. IN	MEAN	% CELL	COLORIMETRIC
PLATE	(uG/mL)	O.D.	CPE	O.D.	VIABILITY	CONTROL
low B	0.625	159	0%	1.088	90%	0.083
C	2	035	0%	1.178	98%	0.063
D	6.2	0.157	17%	0.983	81%	0.047
E	20	321	0%	0.013	1%	0.104
F	62.5	343	0%	029	0%	0.200
high G	200	312	0%	0.007	1%	0.358



DRUG: --- 1924

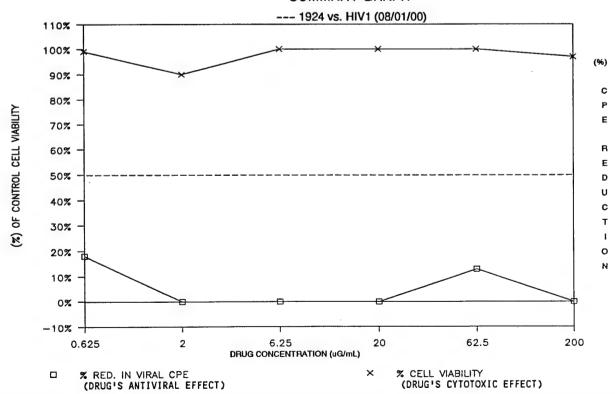
TAI: >3.43

SI: ----

	1	2	3	4	5	6	7	8	9	10	11	12
ſ			reagent back	kground			plastic background					
A	0.393	0.396	0.391	0.393	0.390	0.397	0.043	0.049	0.049	0.049	0.052	0.056
- 1	tox	oc/vc	dru	g 1924 experi	mental	tox					cc/vc	
В	1.385	1.360	1.282	0.625	0.614	1.627					1.452	
C	1.407	1.411	0.629	0.606	0.578	1.417				ł	1.440	
D	1.462	1.566	0.634	0.582	0.690	1.652					1.639	
E	1.534	0.664	0.575	0.701	0.604	1.727					0.613	
F	1.579	0.668	1.125	0.594	0.669	1.697					0.744	
G	1.519	0.665	0.578	0.754	1.074	1.694					0.594	
ı			colorimetric b	ackground								
н	0.559	0.424	0.472	0.465	0.438	0.431						
•	tox=cell to	tox=cell toxicity cc=cell control vc=virus control					= highest dru	g conc		values sho	wn are optica	l densities

VIRUS CELLS SHIPMENT NUMBER STRN	HIV1 CEMSS RF	PASSAGE PASSAGE OPERATOR KMW		PROJECT # SPONSOR TEST DATE DATE READ	 WALTERREED 08/01/00 08/01/00
REAGENT	0.393	DRUG 1924	25%	50%	95%
VIRUS CONTROL	0.265	TC (uG/mL)	> 200.00	> 200.00	> 200.00
CELL CONTROL	1.085	IC (uG/mL)			
DIFFERENTIAL	0.820	ANTIVIRAL INDEX (AI)			

RUG 19	24	ANTIVIRAL TEST VALUES		CYTOTOXICIT	Y TEST VALUES	
ROW ON	CONC.	MEAN	% RED. IN	MEAN	% CELL	COLORIMETRIC
PLATE	(uG/mL)	O.D.	VIRAL CPE	O.D.	VIABILITY	CONTROL
OW B	0.625	0.144	18%	1.075	99%	0.038
С	2	099	0%	0.974	90%	0.045
D	6.25	095	0%	1.092	100%	0.072
Ε	20	110	0%	1.158	100%	0.079
F	62.5	0.107	13%	1.214	100%	0.031
igh G	200	022	0%	1.047	97%	0.166



PLAT	ERFX
DRUG	1025

DIFFERENTIAL

IN VITRO ANTIVIRAL RESULTS XTT ASSAY

ANTIVIRAL INDEX (AI)

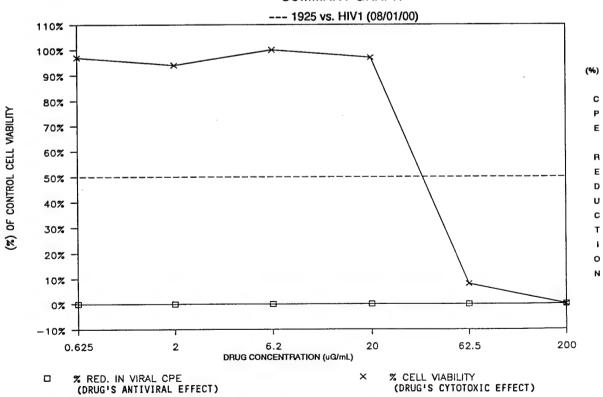
0.820

DRUG: --- 1925 TAI: 0.000000 SI: -----

	1	2	3	4	5	6	7	8	9	10	11	12
			reagent back	ground					plastic backg	round		
	0.393	0.396	0.391	0.393	0.390	0.397	0.043	0.049	0.049	0.049	0.052	0.05
-		oc/vc					tox	dru	g 1925 experi	mental	ec/vc	tox
		1.360					1.532	0.625	0.620	0.742	1.452	1.45
		1.411					1.503	0.563	0.554	0.488	1.440	1.36
	-	1.566			İ		1.586	0.704	0.563	0.601	1.639	1.5
	ı	0.664					1.538	0.508	0.525	0.565	0.613	1.4
		0.668					0.503	0.484	0.421	0.516	0.744	0.5
		0.665					0.436	0.432	0.423	0.464	0.594	0.4
\vdash									colorimetric b	ackground		
1							0.493	0.423	0.427	0.430	0.407	0.4
_	tox=cell to	xicity cc=	cell control	vc=virus co	ntrol	BOLD	= highest dru	ig conc		values sho	wn are optica	d densiti

VIRUS CELLS SHIPMENT NUMBER	HIV1 CEMSS	PASSAGE PASSAGE OPERATOR KMW		PROJECT # SPONSOR TEST DATE	 WALTERREED 08/01/00
STRN	RF			DATE READ	08/01/00
REAGENT	0.393	DRUG 1925	25%	50%	95%
VIRUS CONTROL	0.265	TC (uG/mL)	30.50	42.40	114.00
CELL CONTROL	1.085	IC (uG/mL)			

DRUG 192	5	ANTIVIRAL	TEST VALUES	CYTOTOXICIT		
ROW ON	CONC.	MEAN	% RED. IN	MEAN	% CELL	COLORIMETRIC
PLATE	(uG/mL)	O.D.	CPE	O.D.	VIABILITY	CONTROL
low B	0.625	038	0%	1.056	97%	0.042
С	2	137	0%	1.025	94%	0.014
D	6.2	072	0%	1.119	100%	0.037
Ε	20	159	0%	1.055	97%	0.034
F	62.5	214	0%	0.090	8%	0.030
high G	200	318	0%	031	0%	0.100



TAI: 0.80

SI: ----

	1	2	3	4	5	6	7	8	9	10	11	12
1			reagent back	ground			plastic background					
A	0.436	0.390	0.425	0.417	0.408	0.421	0.054	0.055	0.054	0.056	0.057	0.060
1	tox	oc/vc	dru	1927 experi	imental	tox					cc/vc	
В	1.559	1.573	0.715	0.697	0.695	1.649					1.549	
C	1.543	1.603	0.682	0.696	0.819	1.655					1.612	
D	1.611	1.660	0.608	0.712	0.746	1.844]			L	1.516	
E	1.580	0.705	0.565	0.625	0.555	1.549				:	0.659	
F	0.828	0.731	0.818	0.792	0.823	0.907				l	0.741	
G	0.464	0.602	0.455	0.450	0.445	0.448					0.766	
- 1			colorimetric b	ackground								
н	0.507	0.443	0.430	0.428	0.417	0.432						

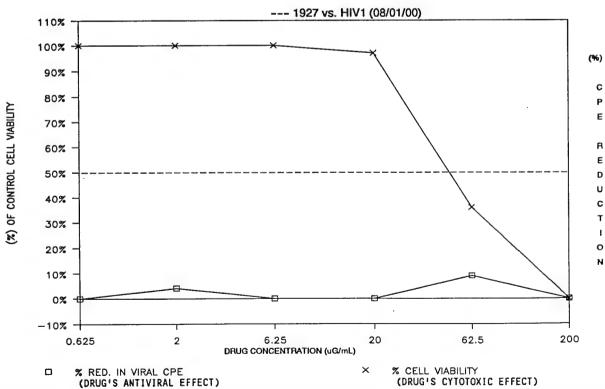
tox=cell toxicity	cc=cell control	vc=virus contro

BOLD = highest drug conc

values shown are optical densities

VIRUS CELLS SHIPMENT NUMBER	HIV1 CEMSS RF	PASSAGE PASSAGE OPERATOR KMW		PROJECT # SPONSOR TEST DATE DATE READ	 WALTERREED 08/01/00 08/01/00
STRN Reagent	0.416	DRUG 1927	25 %	50%	95%
VIRUS CONTROL	0.285	TC (uG/mL)	35.30	52.70	181.00
CELL CONTROL	1.169	IC (uG/mL)			
DIFFERENTIAL	0.885	ANTIVIRAL INDEX (AI)			

DRUG 19	27	ANTIVIRAL	TEST VALUES	CYTOTOXICIT	Y TEST VALUES	
ROW ON	CONC.	MEAN	% RED. IN	MEAN	% CELL	COLORIMETRIC
PLATE	(uG/mL)	O.D.	VIRAL CPE	O.D.	VIABILITY	CONTROL
LOW B	0.625	014	0%	1.172	100%	0.016
С	2	0.031	4%	1.182	100%	0.001
D	6.25	024	0%	1.299	100%	0.012
E	20	133	0%	1.134	97%	0.014
F	62.5	0.083	9%	0.424	36%	0.027
high G	200	342	0%	051	0%	0.091



IN VITRO ANTIVIRAL RESULTS XTT ASSAY

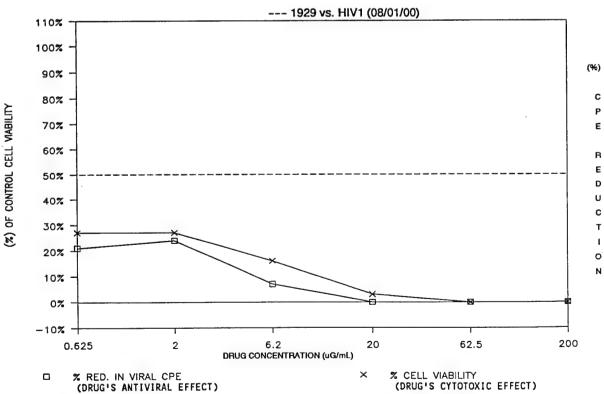
DRUG: --- 1929 TAI: 0.000000 SI: -

	1	2	3	4	5	6	7	8	9	10	11	12
Г			reagent back	ground					plastic backg	round	-	
A	0.436	0.390	0.425	0.417	0.408	0.421	0.054	0.055	0.054	0.056	0.057	0.060
۲		oc/vc					tox	dru	g 1929 experi	mental	cc/vc	tox
3		1.573					0.775	0.900	0.772	1.107	1.549	0.76
		1.603					0.747	0.984	0.985	0.835	1.612	0.77
0		1.660					0.707	0.651	0.960	0.710	1.516	0.53
E	1	0.705					0.439	0.464	0.482	0.507	0.659	0.47
:		0.731					0.403	0.398	0.379	0.412	0.741	0.42
G		0.602					0.468	0.467	0.483	0.487	0.766	0.49
F									colorimetric b	ackground		
н							0.481	0.423	0.421	0.431	0.441	0.454
-	tox=cell to	tox=cell toxicity oc=cell control vc=virus control BOLD = highest drug conc values shown are optical densities										

tox=cell toxicity	y oc=cell control	AC=Alle course

VIRUS	HIV1	PASSAGE		PROJECT #	
CELLS	CEMSS	PASSAGE		SPONSOR	WALTERREED
SHIPMENT NUMBER	••	OPERATOR KMW		TEST DATE	08/01/00
STRN	RF			DATE READ	08/01/00
REAGENT	0.416	DRUG 1929	25 %	50%	95%
VIRUS CONTROL	0.285	TC (uG/mL)	< 0.63	< 0.63	17.90
CELL CONTROL	1.169	IC (uG/mL)			
DIFFERENTIAL	0.885	ANTIVIRAL INDEX (AI)			

DRUG 192	9	ANTIVIRAL TEST VALUES		CYTOTOXICITY	TEST VALUES			
ROW ON	CONC.	MEAN	% RED. IN	MEAN	% CELL	COLORIMETRIC		
PLATE	(uG/mL)	O.D.	CPE	O.D.	VIABILITY	CONTROL		
LOW B	0.625	0.188	21%	0.314	27%	0.038		
С	2	0.209	24%	0.321	27%	0.025		
D	6.2	0.058	7%	0.188	16%	0.015		
E	20	221	0%	0.034	3%	0.005		
F	62.5	311	0%	011	0%	0.007		
high G	200	287	0%	0.000	0%	0.065		



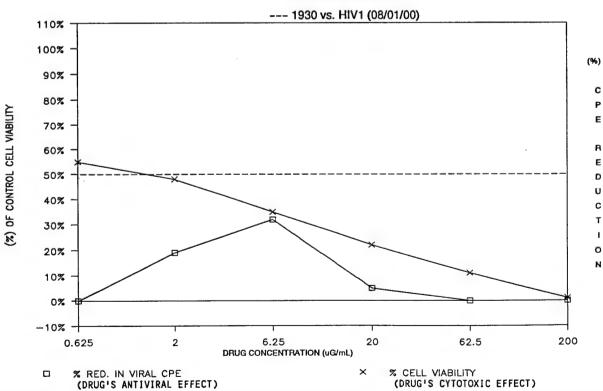
DRUG: ---- 1930

TAI: 0.000000 SI: -

	1	2	3	4	5	6	7	8	9	10	_ 11	12
ſ	reagent background								plastic backg	round		
A	0.425	0.421	0.433	0.451	0.437	0.457	0.067	0.070	0.067	0.070	0.073	0.075
1	tox	oc/vc	dru	g 1930 experi	mental	tox					cc/vc	
В	1.024	1.436	0.596	0.639	0.814	1.017					1.627	
C	0.875	1.495	0.894	0.879	0.784	0.975					1.697	
D	0.793	1.643	1.016	0.970	1.085	0.863					1.728	
E	0.721	0.940	0.830	0.950	0.706	0.691				ſ	0.727	
F	0.695	0.581	0.820	0.928	0.883	0.733				1	0.671	
G	1.007	0.956	0.991	1.047	1.003	1.020					0.746	
- 1	colorimetric background											
н	1.005	0.591	0.455	0.422	0.364	0.383						
•	tox=cell toxicity cc=cell control vc=virus control					BOLD	= highest dru	g conc		values sho	wn are optica	densities

VIRUS CELLS SHIPMENT NUMBER STRN	HIV1 CEMSS RF	PASSAGE PASSAGE OPERATOR KMW		PROJECT # SPONSOR TEST DATE DATE READ	WALTERREED 08/01/00 08/01/00	
REAGENT	0.437	DRUG 1930	25%	50%	95%	
VIRUS CONTROL	0.333	TC (uG/mL)	< 0.63	1.61	145.00	
CELL CONTROL	1.167	IC (uG/mL)	3.38			
DIFFERENTIAL	0.834	ANTIVIRAL INDEX (AI)	< 0.18			

DRUG 193	0	ANTIVIRAL	TEST VALUES	CYTOTOXICIT	Y TEST VALUES	
ROW ON	CONC.	MEAN	% RED. IN	MEAN	% CELL	COLORIMETRIC
PLATE	(uG/mL)	O.D.	VIRAL CPE	O.D.	VIABILITY	CONTROL
low B	0.625	033	0%	0.637	55%	054
C	2	0.155	19%	0.561	48%	073
D	6.25	0.268	32%	0.406	35%	015
Ε	20	0.040	5%	0.251	22%	0.018
F	62.5	047	0%	0.123	11%	0.154
nigh G	200	325	0%	0.008	1%	0.568



MDHO

DRUG: --- 1932

TAI: 3.39

SI: ----

	1	2	3	4	5	6	7	8	9	10	11 -	12
Г			reagent back	ground					plastic backg	round		
A	0.425	0.421	0.433	0.451	0.437	0.457	0.067	0.070	0.067	0.070	0.073	0.075
Г		cc/vc					tox	dru	1932 experi	mental	cc/vc	tox
В		1.436					1.588	0.669	0.668	0.661	1.627	1.642
C	j	1.495					1.713	0.713	0.652	1.265	1.697	1.712
D	l	1.643					1.728	0.709	0.772	0.646	1.728	1.625
E		0.940					1.555	0.669	0.617	0.609	0.727	1.522
F		0.581					1.016	0.858	1.025	1.189	0.671	1.473
G		0.956					0.683	0.668	0.688	0.654	0.746	0.663
Г					-				colorimetric b	ackground		
H							0.631	0.446	0.396	0.388	0.399	0.424

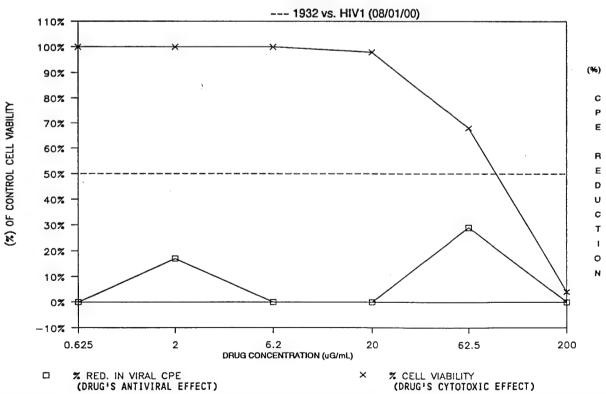
tox=cell toxicity	cc=cell control	vc=virus control
DUIG	LIIV/4	0400405

BOLD = highest drug conc

values shown are optical densities

VIRUS	LIIA !	PASSAGE		PROJECT #	
CELLS	CEMSS	PASSAGE		SPONSOR	WALTERREED
SHIPMENT NUMBER		OPERATOR KMW		TEST DATE	08/01/00
STRN	RF			DATE READ	08/01/00
REAGENT	0.437	DRUG 1932	25%	50%	95%
VIRUS CONTROL	0.333	TC (uG/mL)	52.60	101.00	198.00
CELL CONTROL	1.167	IC (uG/mL)	53.40		
DIFFERENTIAL	0.834	ANTIVIRAL INDEX (AI)	0.98		

DRUG '	1932	2	ANTIVIRAL TEST VALUES		CYTOTOXICITY	TEST VALUES	
ROW (ON	CONC.	MEAN	% RED. IN	MEAN	% CELL	COLORIMETRIC
PLA	TE	(uG/mL)	O.D.	CPE	O.D.	VIABILITY	CONTROL
LOW E	В	0.625	091	0%	1.191	100%	013
	C	2	0.144	17%	1.313	100%	038
0	o i	6.2	012	0%	1.288	100%	049
1	E	20	097	0%	1.142	98%	041
(F	62.5	0.245	29%	0.798	68%	0.009
high (G	200	294	0%	0.042	4%	0.194



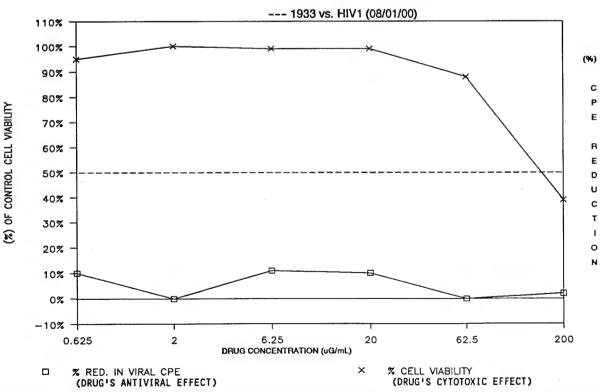
DRUG: ---- 1933 TAI: >3.79

SI: ---

	1	2	3	4	5	6	7	8	9	10	11	12
			reagent back	ground					plastic backg	round		
A	0.405	0.358	0.394	0.400	0.390	0.432	0.042	0.047	0.046	0.046	0.052	0.061
1	tox	oc/vo	dru	g 1933 experi	mental	tox					cc/vc	
В	1.614	1.572	0.746	1.104	0.713	1.616	l			1	1.670	
C	1.590	1.554	0.633	0.708	0.653	1.788	ŀ				1.744	
D	1.616	1.650	0.647	0.786	1.141	1.705				1	1.692	
E	1.626	0.820	0.650	1.237	0.656	1.700				[0.771	
F	1.523	0.729	0.593	0.618	0.621	1.565					0.753	
G	0.757	0.641	0.949	1.054	0.658	1.303					0.677	
- 1			colorimetric b	ackground								
H	0.537	0.441	0.423	0.424	0.406	0.426						
•	tox=cell to	tox=cell toxicity cc=cell control vc=virus control					- highest dru	ig conc		values sho	wn are optica	l densities

VIRUS	HIV1	PASSAGE		PROJECT #	
CELLS	CEMSS	PASSAGE		SPONSOR	WALTERREED
SHIPMENT NUMBER		OPERATOR KMW		TEST DATE	08/01/00
STRN	RF			DATE READ	08/01/00
REAGENT	0.397	DRUG 1933	25 %	50%	95%
VIRUS CONTROL	0.335	TC (uG/mL)	99.00	169.00	> 200.00
CELL CONTROL	1.251	IC (uG/mL)			
DIFFERENTIAL	0.915	ANTIVIRAL INDEX (AI)			

DRUG	193	3	ANTIVIRAL	TEST VALUES	CYTOTOXICITY	TEST VALUES	
ROW	ON	CONC.	MEAN	% RED. IN	MEAN	% CELL	COLORIMETRIC
PLA	TE	(uG/mL)	O.D.	VIRAL CPE	O.D.	VIABILITY	CONTROL
low	В	0.625	0.094	10%	1.190	95%	0.029
	C	2	077	0%	1.283	100%	0.010
	D	6.25	0.099	11%	1.237	99%	0.027
	E	20	0.090	10%	1.241	99%	0.026
	F	62.5	165	0%	1.104	88%	0.044
high	G	200	0.014	2%	0.492	39%	0.141



TAI: 1.38

Si: ----

0.405	0.358 cc/vc	eagent back 0.394	ground 0.400	0.390				lastic backgi	round		
0.405		0.394	0.400	0.700					04114		
	oc/vc			0.370	0.432	0.042	0.047	0.046	0.046	0.052	0.061
						tox	drug	1936 experi	mental	oc/vc	tox
	1.572					1.622	0.751	0.777	0.902	1.670	1.702
- 1	1.554					1.774	0,782	0.748	0.960	1.744	1.731
1	1.650					1.722	0.723	0.710	0.707	1.692	1.673
Ī	0.820			l		1.728	0.615	0.661	0.706	0.771	1.793
	0.729					0.963	0.550	0.631	0.552	0.753	1.154
- 1	0.641					0.533	0.505	0.528	0.508	0.677	0.549
	•							colorimetric b	ackground		
						0.565	0.454	0.434	0.431	0.426	0.463
		0.820 0.729	0.820 0.729	0.820 0.729	0.820 0.729	0.820 0.729	0.820 1.728 0.729 0.963 0.641 0.533	0.820 1.728 0.615 0.729 0.963 0.550 0.641 0.533 0.505	0.820 1.728 0.615 0.661 0.729 0.963 0.550 0.631 0.641 0.533 0.505 0.528	0.820 1.728 0.615 0.661 0.706 0.729 0.963 0.550 0.631 0.552 0.641 0.533 0.505 0.528 0.508	0.820 1.728 0.615 0.661 0.706 0.771 0.729 0.963 0.550 0.631 0.552 0.753 0.641 0.533 0.505 0.528 0.508 0.677

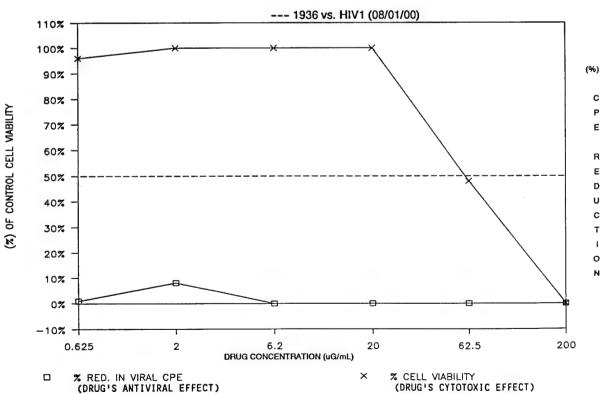
tox=cell toxicity cc=cell control vc=virus control

BOLD = highest drug conc

values shown are optical densities

VIRUS CELLS SHIPMENT NUMBER STRN	HIV1 CEMSS RF	PASSAGE PASSAGE OPERATOR KMW	PROJECT # SPONSOR TEST DATE DATE READ	WALTERREED 08/01/00 08/01/00	
REAGENT	0.397	DRUG 1936	25%	50%	95%
VIRUS CONTROL	0.335	TC (uG/mL)	40.40	60.90	186.00
CELL CONTROL	1.251	IC (uG/mL)			
DIFFERENTIAL	0.915	ANTIVIRAL INDEX (AI)			

DRUG	193	6	ANTIVIRAL	TEST VALUES	CYTOTOXICITY	TEST VALUES	
ROW	ON	CONC.	MEAN	% RED. IN	MEAN	% CELL	COLORIMETRIC
PLA	ATE	(uG/mL)	O.D.	CPE	O.D.	VIABILITY	CONTROL
low	В	0.625	0.011	1%	1.199	96%	0.067
	C	2	0.069	8%	1.327	100%	0.029
	D	6.2	053	0%	1.267	100%	0.034
	E	20	108	0%	1.327	100%	0.037
	F	62.5	212	0%	0.604	48%	0.058
high	G	200	386	0%	023	0%	0.168



DIFFERENTIAL

0.928

IN VITRO ANTIVIRAL RESULTS XTT ASSAY

ANTIVIRAL INDEX (AI)

DRUG: --- 1946 TAI: >14.67

SI: ---

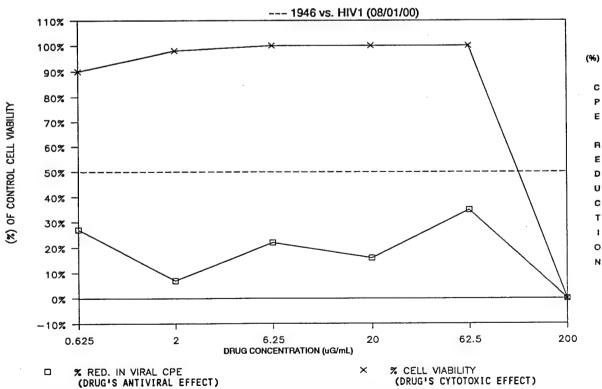
	1	2	3	4	5	6	7	8	9	10	11	12
ſ			reagent back	ground					plastic backg	round		
A	0.419	0.387	0.416	0.403	0.394	0.414	0.043	0.048	0.043	0.051	0.051	0.059
1	tox	ec/vc	dru	g 1946 experi	mental	tox					cc/vc	
В	1.477	1.534	0.726	1.484	0.648	1.553					1.584	
C	1.596	1.614	0.717	0.876	0.676	1.594					1.632	
D	1.744	1.687	0.692	1.032	1.050	1.753					1.670	
Е	1.707	0.715	1.215	0.684	0.708	1.707	i				0.687	
F	1.778	0.727	0.974	1.433	0.786	1.857					0.654	
G	0.458	0.664	0.449	0.457	0.432	0.428					0.709	
	•		colorimetric t	ackground								
н	0.505	0.452	0.433	0.437	0.409	0.418						
	tox=cell to	tox=cell toxicity oc=cell control vc=virus control					- highest dru	ig conc		values sho	wn are optica	densities

VIRUS	HIV1	PASSAGE		PROJECT #	

CELLS	CEMSS	PASSAGE		SPONSOR	WALTERREED
SHIPMENT NUMBER		OPERATOR KMW		TEST DATE	08/01/00
STRN	RF			DATE READ	08/01/00
REAGENT	0.406	DRUG 1946	25%	50%	95%
VIRUS CONTROL	0.287	TC (uG/mL)	96.90	131.00	193.00
CELL CONTROL	1.215	IC (uG/mL)	< 0.63		

DRUG	194	6	ANTIVIRAL	TEST VALUES	CYTOTOXICITY	TEST VALUES	
ROW		CONC.	MEAN	% RED. IN	MEAN	% CELL	COLORIMETRIC
	ATE	(uG/mL)	O.D.	VIRAL CPE	O.D.	VIABILITY	CONTROL
low	В	0.625	0.248	27%	1.098	90%	0.012
	С	2	0.061	7%	1.187	98%	0.003
	D	6.25	0.200	22%	1.311	100%	0.032
	Ε	20	0.149	16%	1.275	100%	0.027
	F	62.5	0.325	35%	1.365	100%	0.047
high	G	200	347	0%	063	0%	0.100

155.00



TAI: 8.65

DRUG: --- 1948 .65 SI: 1.88

	1	2	3	4	5	6	7	8	9	10	11	12
Г			reagent back	ground			plastic background					
A	0.419	0.387	0.416	0.403	0.394	0.414	0.043	0.048	0.043	0.051	0.051	0.059
		oc/vc					tox	dru	1948 experi	mental	cc/vc	tox
В		1.534					1.536	0.710	0.690	0.705	1.584	1.613
C	1	1.614					1.649	0.787	0.687	0.752	1.632	1.638
D		1.687					1.788	0.722	0.743	0.625	1.670	1.671
E		0.715					1.334	1.553	1.682	0.986	0.687	1.744
F		0.727				1	0.453	0.451	0.464	0.433	0.654	0.490
G		0.664					0.608	0.563	0.601	0.573	0.709	0.613
Ī									colorimetric b	ackground		
H							0.626	0.484	0.459	0.432	0.431	0.454

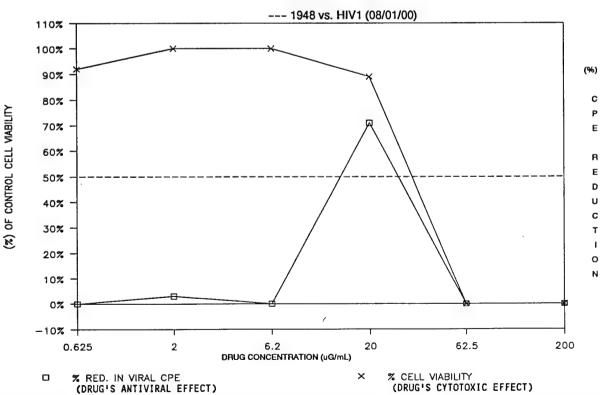
tox=cell toxicity	cc=cell control	vc=virus control

BOLD = highest drug conc

values shown are optical densities

VIRUS	HIV1	PASSAGE		PROJECT #	
CELLS	CEMSS	PASSAGE		SPONSOR	WALTERREED
SHIPMENT NUMBER		OPERATOR KMW		TEST DATE	08/01/00
STRN	RF			DATE READ	08/01/00
REAGENT	0.406	DRUG 1948	25%	50%	95 X
VIRUS CONTROL	0.287	TC (uG/mL)	26.70	38.60	60.10
CELL CONTROL	1.215	IC (uG/mL)	9.41	14.20	
DIFFERENTIAL	0.928	ANTIVIRAL INDEX (AI)	2.83	2.72	

DRUG 194	8	ANTIVIRAL	TEST VALUES	CYTOTOXICITY	TEST VALUES	
ROW ON	CONC.	MEAN	% RED. IN	MEAN	% CELL	COLORIMETRIC
PLATE	(uG/mL)	O.D.	CPE	O.D.	VIABILITY	CONTROL
low B	0.625	040	0%	1.120	92%	0.049
C	2	0.024	3%	1.213	100%	0.025
D	6.2	022	0%	1.298	100%	0.026
E	20	0.660	71%	1.080	89%	0.054
F	62.5	321	0%	012	0%	0.078
high G	200	335	0%	016	0%	0.221



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ANTIVIRAL INDEX (AI)

TAI: >1.62

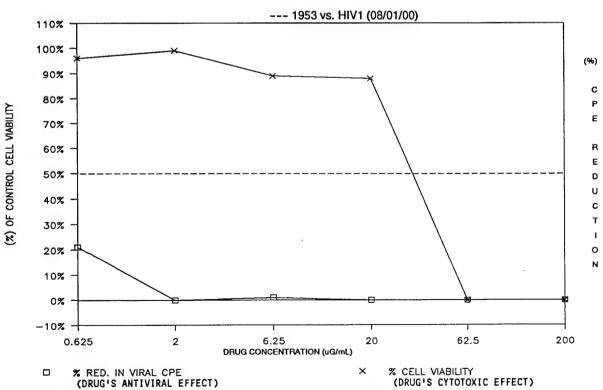
DRUG: --- 1953

	1	2	3	4	5	6	7	8	9 .	10	11	12
ſ			reagent back	ground					plastic backg	round		-
A	0.420	0.409	0.390	0.410	0.415	0.418	0.047	0.051	0.051	0.051	0.054	0.060
- 1	tox										cc/vc	
В	1.621	1.647	1.482	0.655	0.690	1.700					1.584	
ε	1.671	1.705	0.710	0.702	0.656	1.764					1.718	
D	1.616	1.732	0.986	0.725	0.775	1.666	.			1	1.703	
E	1.702	0.705	0.931	0.803	0.732	1.793	1			[0.745	
F	0.865	0.667	0.840	0.849	0.844	0.878					0.726	
G	0.976	0.759	0.959	0.977	0.984	0.962					0.711	
			colorimetric t	ackground								
н	1.020	0.903	0.624	0.506	0.459	0.436						
	tox=cell toxicity cc=cell control vc=virus control					BOLD	= highest dru	g conc		values sho	wn are optica	l densities

VIRUS	HIV1
CELLS	CEMSS
SHIPMENT NUMBER	
STRN	RF
REAGENT	0.410
VIRUS CONTROL	0.309
CELL CONTROL	1.271
DIFFERENTIAL	0.963

HIV1	PASSAGE		PROJECT #	••
CEMSS	PASSAGE		SPONSOR	WALTERREED
	OPERATOR KMW		TEST DATE	08/01/00
RF			DATE READ	08/01/00
0.410	DRUG 1953	25%	50 X	95%
0.309	TC (uG/mL)	26.30	38.40	60.10
1.271	IC (uG/mL)			

DRUG 19	253	ANTIVIRAL	TEST VALUES	CYTOTOXICITY	TEST VALUES	
ROW OF			% RED. IN	MEAN	% CELL	COLORIMETRIC
PLATE			VIRAL CPE	O.D.	VIABILITY	CONTROL
low B	0.625	0.198	21%	1.224	96%	0.026
C	2	079	0%	1.258	99%	0.049
D	6.25	0.014	1%	1.135	89%	0.096
E	20	111	0%	1.123	88%	0.214
F	62.5	368	0%	032	0%	0.493
high G	200	356	0%	051	0%	0.610

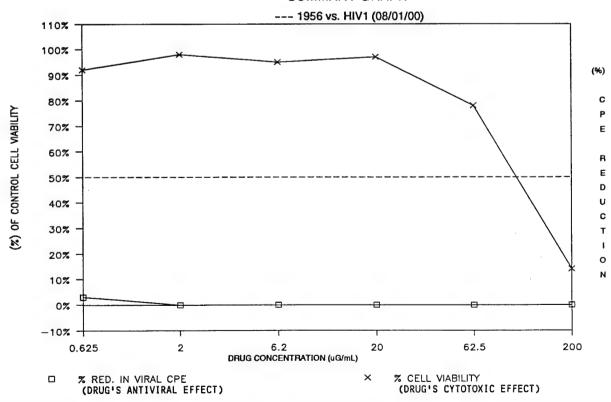


DRUG: --- 1956 TAI: 0.000000 SI: ----

	1	2	3	4	5	6	7	8	9	10	11	12
Г			reagent back	ground					plastic backg	round		
A	0.420	0.409	0.390	0.410	0.415	0.418	0.047	0.051	0.051	0.051	0.054	0.060
Г		oc/vc					tox	drug	1956 experi	mental	cc/vc	tox
В		1.647					1.677	0.879	0.706	0.796	1.584	1.563
C		1.705					1.642	0.695	0.650	0.668	1.718	1.690
D		1.732					1.681	0.708	0.655	0.621	1.703	1.575
E	ſ	0.705					1.697	0.635	0.681	0.754	0.745	1.634
F		0.667					1.479	0.599	0.578	0.600	0.726	1.432
G		0.759					0.655	0.642	0.637	0.713	0.711	0.842
									colorimetric b	ackground		
H							0.571	0.469	0.433	0.425	0.420	0.452
_	tox=cell toxicity cc=cell control vc=virus control BOLD = highest drug conc values shown are optical densities											

VIRUS	HIV1	PASSAGE		PROJECT #	••
CELLS	CEMSS	PASSAGE		SPONSOR	WALTERREED
SHIPMENT NUMBER		OPERATOR KMW		TEST DATE	08/01/00
STRN	RF			DATE READ	08/01/00
REAGENT	0.410	DRUG 1956	25%	50%	95%
VIRUS CONTROL	0.309	TC (uG/mL)	68.90	123.00	> 200.00
CELL CONTROL	1.271	IC (uG/mL)			
DIFFERENTIAL	0.963	ANTIVIRAL INDEX (AI)			

DRUG 1	1956		ANTIVIRAL	TEST VALUES	CYTOTOXICITY	TEST VALUES	
ROW (ON C	ONC.	MEAN	% RED. IN	MEAN	% CELL	COLORIMETRIC
PLAT	TE (uc	(Jm/a	O.D.	CPE	0.0.	VIABILITY	CONTROL
low E	3 0.	625	0.033	3%	1.168	92%	0.042
(:	2	058	0%	1.246	98%	0.010
)	6.2	072	0%	1.203	95%	0.015
1 1	:	20	052	0%	1.232	97%	0.023
	F 6	52.5	186	0%	0.986	78%	0.059
high (3	200	216	0%	0.177	14%	0.161



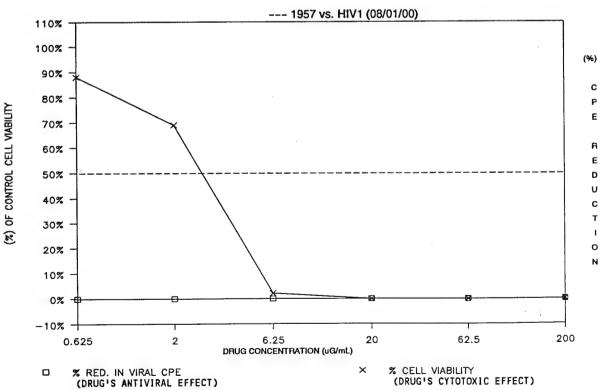
IN VITRO ANTIVIRAL RESULTS XTT ASSAY

DRUG: --- 1957 TAI: 0.000000 SI: ----

	1	2	3	4	5	6	7	8	9	10	11	12
ſ			reagent back	ground			plastic background					
Ā	0.434	0.422	0.407	0.415	0.430	0.447	0.056	0.059	0.056	0.059	0.064	0.065
1	tox	oc/vc	dru	g 1957 experi	mental	tox					ec/vc	
В	1.489	1.656	0.573	0.560	0.611	1.539	i .				1.634	
С	1.238	1.612	0.692	0.633	0.573	1.260					1.646	
D	0.452	1.647	0.380	0.400	0.404	0.451				l	1.670	
Ε	0.405	0.693	0.346	0.367	0.371	0.394					0.695	
F	0.456	0.729	0.409	0.424	0.416	0.427					0.828	
G	0.507	0.687	0.464	0.526	0.463	0.488					0.745	
- 1	colorimetric background											
н	0.543	0.464	0.426	0.431	0.407	0.445						
	tox-cell to	ec=	call control	vc=virus co	ntrol	BOLD	- highest dru	ig conc		values sho	wn are optica	densities

VIRUS	HIV1	PASSAGE		PROJECT #	
CELLS	CEMSS	PASSAGE		SPONSOR	WALTERREED
SHIPMENT NUMBER		OPERATOR KMW		TEST DATE	08/01/00
STRN	RF			DATE READ	08/01/00
REAGENT	0.426	DRUG 1957	25%	50%	95%
VIRUS CONTROL	0.304	TC (uG/mL)	1.57	3.21	6.06
CELL CONTROL	1.218	IC (uG/mL)			
DIFFERENTIAL	0.915	ANTIVIRAL INDEX (AI)			

DRUG 195	7	ANTIVIRAL	TEST VALUES	CYTOTOXICITY	TEST VALUES	
ROW ON	CONC.	MEAN	% RED. IN	MEAN	% CELL	COLORIMETRIC
PLATE	(uG/mL)	0.0.	VIRAL CPE	O.D.	VIABILITY	CONTROL
low B	0.625	167	0%	1.069	88%	0.019
C	2	078	0%	0.842	69%	019
D	6.25	340	0%	0.021	2%	0.005
E	20	368	0%	026	0%	0.000
F	62.5	351	0%	022	0%	0.038
high G	200	362	0%	045	0%	0.117



CELL CONTROL DIFFERENTIAL DRUG: --- 1958

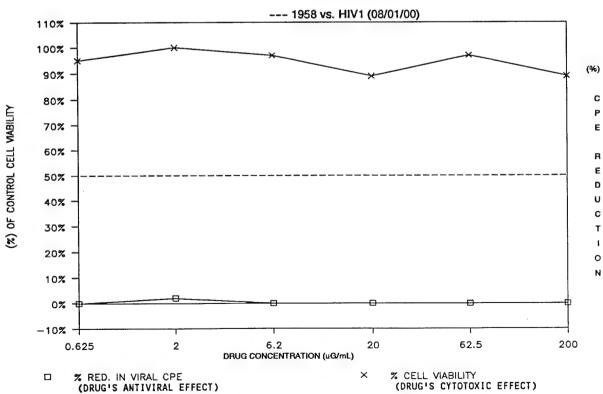
	Drog.	,	330
TAI: 0	.14	SI:	

1	2	3	4	5	6	7	8	9	10	11	12
		reagent back	ground					plastic backg	round		
0.434	0.422	0.407	0.415	0.430	0.447	0.056	0.059	0.056	0.059	0.064	0.06
	oc/vc			T I		tox	dru	g 1958 experi	mentai	cc/vc	tox
	1.656			İ		1.623	0.740	0.697	0.729	1.634	1.594
	1.612					1.709	0.736	0.710	0.721	1.646	1.693
	1.647					1.555	0.733	0.769	0.691	1.670	1.67
	0.693					1.521	0.641	0.649	0.665	0.695	1.51
	0.729					1.638	0.646	0.647	0.645	0.828	1.568
	0.687					1.572	0.547	0.608	0.602	0.745	1.466
								colorimetric b	ackground		
						0.430	0.425	0.429	0.431	0.399	0.452
tox=ce	Il toxicity cc=	cell control	vc=virus co	ntrol	BOLD	- highest dru	ig conc		values sho	wn are optica	densities

VIRUS CELLS SHIPMENT NUMBER STRN	HIV1 CEMSS RF	PASSAGE PASSAGE OPERATOR KMW	PROJECT # SPONSOR TEST DATE DATE READ	 WALTERREED 08/01/00 08/01/00
REAGENT	0.426	DRUG 1958 25%	50 X	95%
VIRUS CONTROL	0.304	TC (uG/mL) > 200.00	> 200.00	> 200.00

304	TC (uG/mL)	> 200.00	> 200.00 > 200.00
1.218	IC (uG/mL)		
0.915	ANTIVIRAL INDEX (AI)		

DRUG 195	8	ANTIVIRAL	TEST VALUES	CYTOTOXICIT	Y TEST VALUES	
ROW ON	CONC.	MEAN	% RED. IN	MEAN	% CELL	COLORIMETRIC
PLATE	(uG/mL)	O.D.	CPE	O.D.	VIABILITY	CONTROL
Low B	0.625	034	0%	1.157	95%	0.026
C	2	0.020	2%	1.302	100%	027
D	6.2	004	0%	1.183	97%	0.005
E	20	081	0%	1.090	89%	0.003
F	62.5	082	0%	1.178	97%	001
high G	200	148	0%	1.089	89%	0.004



DRUG: --- 1959

TAI: 6.20

SI: ----

	1	2	3	4	5	6	7	8	9	10	11	12
- 1	reagent background							plastic backg	round			
A	0.467	0.448	0.465	0.457	0.443	0.451	0.062	0.067	0.066	0.070	0.071	0.075
	tox	oc/vc	oc/vc drug 1959 experimental			tox				,	cc/vc	
В	1.462	1.626	0.757	0.688	0.808	1.639	l				1.712	
С	1.403	1.565	0.690	0.692	0.692	1.335					1.640	
D	1.618	1.788	1.400	0.930	0.922	1.485					1.784	
E	1.716	0.783	0.622	1.116	1.346	1.869					0.821	
F	0.556	0.786	0.538	0.558	0.583	0.608					0.734	
G	0.398	0.650	0.390	0.391	0.398	0.406					1.041	
			colorimetric b	ackground								
н	0.417	0.422	0.431	0.466	0.455	0.456						

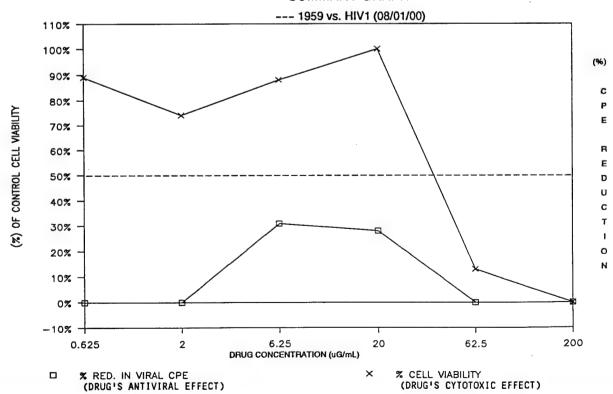
tox=cell toxicity	cc=cell control	vc=virus control

BOLD - highest drug conc

values shown are optical densities

VIRUS	HIV1	PASSAGE		PROJECT #		
CELLS	CEMSS	PASSAGE		SPONSOR	WALTERREED	
SHIPMENT NUMBER	••	OPERATOR KMW		TEST DATE	08/01/00	
STRN	RF			DATE READ	08/01/00	
REAGENT	0.455	DRUG 1959	25%	50%	95%	
VIRUS CONTROL	0.347	TC (uG/mL)	1.91	44.40	147.00	
CELL CONTROL	1.231	IC (uG/mL)	5.01			
DIFFERENTIAL	0.883	ANTIVIRAL INDEX (AI)	0.38		H====	

DRUG 195	9	ANTIVIRAL	TEST VALUES	CYTOTOXICITY	CYTOTOXICITY TEST VALUES	
ROW ON	CONC.	MEAN	% RED. IN	MEAN	% CELL	COLORIMETRIC
PLATE	(uG/mL)	O.D.	VIRAL CPE	0.0.	VIABILITY	CONTROL
low B	0.625	052	0%	1.094	89%	0.001
С	2	111	0%	0.914	74%	0.000
D	6.25	0.271	31%	1.085	88%	0.011
E	20	0.250	28%	1.361	100%	024
F	62.5	210	0%	0.160	13%	033
high G	200	372	0%	015	0%	038



DRUG: --- 1960 TAI: 12.87 SI: ----

	1	2	3	4	5	6	7	8	9	10	11	12
			reagent back	ground					plastic backg	round		
١l	0.467	0.448	0.465	0.457	0.443	0.451	0.062	0.067	0.066	0.070	0.071	0.07
		ec/vc					tox	dru	g 1960 experi	mental	cc/vc	tox
3	.	1.626					1.767	0.707	0.840	0.774	1.712	1.648
:		1.565					1.709	1.434	1.242	0.803	1.640	1.65
		1.788			i		1.829	1.403	0.723	0.712	1.784	1.74
		0.783					1.877	0.897	0.852	0.852	0.821	1.75
:		0.786					1.740	0.612	0.743	0.783	0.734	1.66
:		0.650					1.770	0.746	0.649	0.659	1.041	1.66
									colorimetric b	ackground		
1							0.455	0.455	0.449	0.456	0.450	0.494
	tox=cell to	ox-cell toxicity oc-cell control vc-virus control BOLD - highest drug conc values shown are optical densities										

VIRUS CELLS SHIPMENT NUMBER		PASSAGE PASSAGE OPERATOR KMW		PROJECT # SPONSOR TEST DATE	WALTERREED 08/01/00
STRN	RF			DATE READ	08/01/00
REAGENT	0.455	DRUG 1960	25%	50%	95%
VIRUS CONTROL	0.347	TC (uG/mL)	> 200.00	> 200.00	> 200.00
CELL CONTROL	1.231	IC (uG/mL)	1.27		
DIFFERENTIAL	0.883	ANTIVIRAL INDEX (AI)	> 157.45		

DRUG 196	0	ANTIVIRAL	TEST VALUES	CYTOTOXICITY		
ROW ON	CONC.	MEAN	% RED. IN	MEAN	% CELL	COLORIMETRIC
PLATE	(uG/mL)	O.D.	CPE	O.D.	VIABILITY	CONTROL
low B	0.625	068	0%	1.213	99%	0.039
C	2	0.362	41%	1.233	100%	005
D	6.2	0.142	16%	1.332	100%	0.001
E	20	0.071	8%	1.367	100%	006
F	62.5	090	0%	1.245	100%	0.000
high G	200	118	0%	1.262	100%	0.000

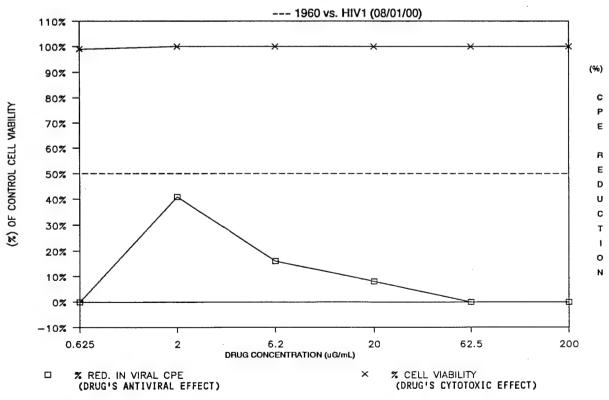


PLATE RG5 DRUG 1961

IN VITRO ANTIVIRAL RESULTS XTT ASSAY

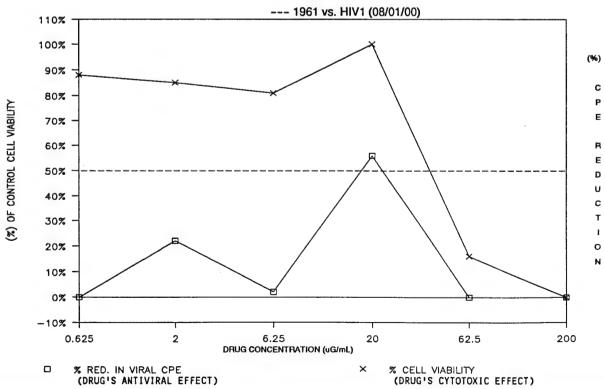
TAI: 7.01

DRUG: --- 1961 SI: 1.86

	1	2	3	4	5	6	7	8	9	10	11	12
			reagent back	kground					plastic backgi	round		
A	0.434	0.421	0.427	0.440	0.413	0.445	0.059	0.060	0.059	0.055	0.058	0.061
	tox	ec/vc	dru	g 1961 experi	mental	tox			·		cc/vc	
В	1.452	1.610	0.691	0.685	0.677	1.672					1.866	
C	1.458	1.669	0.735	0.672	1.474	1.588					1.815	
D	1.581	1.577	0.673	0.834	0.815	1.377					1.747	
E	1.817	0.731	1.732	1.041	1.158	1.689					0.659	
F	0.598	0.628	0.696	0.762	0.760	0.725					0.778	
G	0.551	0.814	0.536	0.515	0.516	0.523					0.859	
			colorimetric b	ackground								
H	0.569	0.459	0.451	0.441	0.428	0.436						
	tov-cell to	nvicity oc-	cell control	ve-virue cor	atrol	ROI D	- highest dry	o conc		values ebo	wn are entice	Idensities

VIRUS	HIV1	PASSAGE		PROJECT #	••
CELLS	CEMSS	PASSAGE		SPONSOR	WALTERREED
SHIPMENT NUMBER	••	OPERATOR KMW		TEST DATE	08/01/00
STRN	RF			DATE READ	08/01/00
REAGENT	0.430	DRUG 1961	25%	50%	95%
VIRUS CONTROL	0.315	TC (uG/mL)	32.60	45.30	157.00
CELL CONTROL	1.284	IC (uG/mL)	10.30	17.60	
DIFFERENTIAL	0.969	ANTIVIRAL INDEX (AI)	3.18	2.58	

DRUG 196	1	ANTIVIRAL	TEST VALUES	CYTOTOXICITY	TY TEST VALUES		
ROW ON	CONC.	MEAN	% RED. IN	MEAN	% CELL	COLORIMETRIC	
PLATE	(uG/mL)	O.D.	VIRAL CPE	O.D.	VIABILITY	CONTROL	
low B	0.625	067	0%	1.126	88%	0.006	
C	2	0.217	22%	1.095	85%	002	
. D	6.25	0.018	2%	1.038	81%	0.011	
E	20	0.544	56%	1.302	100%	0.021	
F	62.5	035	0%	0.202	16%	0.029	
high G	200	362	0%	032	0%	0.139	



IN VITRO ANTIVIRAL RESULTS XTT ASSAY

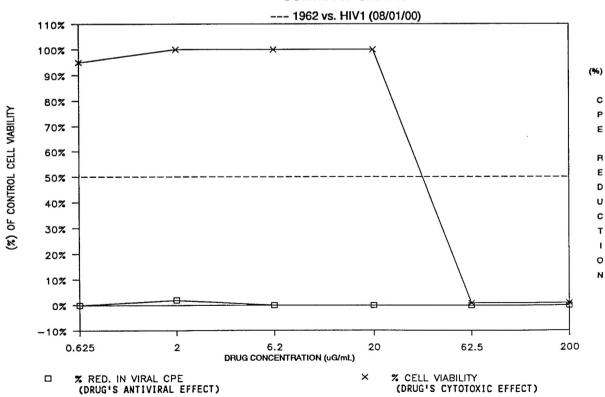
TAI: 0.26

DRUG: --- 1962 .26 SI: ----

	1	2	3	4	5	6	7	8	9	10	11	12
Г			reagent back	ground				1	plastic backg	round		
A	0.434	0.421	0.427	0.440	0.413	0.445	0.059	0.060	0.059	0.055	0.058	0.061
- 1		ec/vc					tox	dru	1962 experi	mental	cc/vc	tox
В	1	1.610					1.755	1.006	0.754	0.656	1.866	1.672
С		1.669					1.686	0.826	0.738	0.731	1.815	1.814
D		1.577					1.843	0.879	0.697	0.679	1.747	1.746
E	ſ	0.731					1.820	0.664	0.715	0.813	0.659	1.745
F		0.628					0.438	0.486	0.460	0.509	0.778	0.526
G		0.814					0.507	0.474	0.464	0.464	0.859	0.495
1									colorimetric b	ackground		
H							0.491	0.473	0.457	0.457	0.430	0.490
•	tox=cell toxicity cc=cell control vc=virus control BOL						= highest dru	g conc		values sho	wn are optica	l densities

1011-1011		-			•	
VIRUS	HIV1	PASSAGE		PROJECT #		
CELLS	CEMSS	PASSAGE		SPONSOR	WALTERREED	
SHIPMENT NUMBER		OPERATOR KMW		TEST DATE	08/01/00	
STRN	RF			DATE READ	08/01/00	
REAGENT	0.430	DRUG 1962	25%	50%	95%	
VIRUS CONTROL	0.315	TC (uG/mL)	30.70	41.50	60.80	
CELL CONTROL	1.284	IC (uG/mL)				
DIFFERENTIAL	0.969	ANTIVIRAL INDEX (AI)				

DRUG 196	2	ANTIVIRAL	TEST VALUES	CYTOTOXICIT	Y TEST VALUES	
ROW ON	CONC.	MEAN	% RED. IN	MEAN	% CELL	COLORIMETRIC
PLATE	(uG/mL)	O.D.	CPE	O.D.	VIABILITY	CONTROL
low B	0.625	0.001	0%	1.224	95%	0.060
C	2	0.020	2%	1.320	100%	0.000
D	6.2	020	0%	1.338	100%	0.027
E	20	041	0%	1.326	100%	0.027
F	62.5	303	0%	0.009	1%	0.043
high G	200	339	0%	0.010	1%	0.061

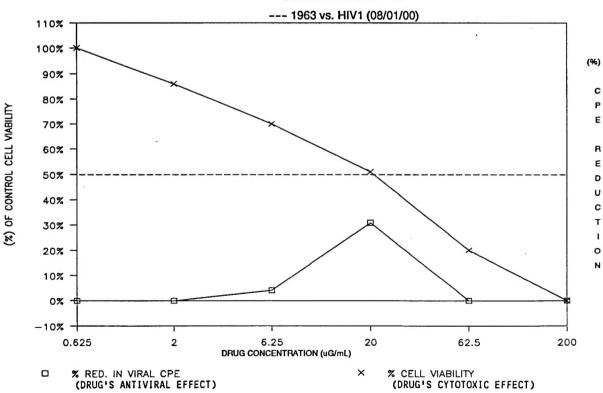


DRUG: --- 1963 TAI: 0.000000 SI: ----

	1	2	3	4	5	6	7	8	9	10	11	12
			reagent back	kground					plastic backg	round		
	0.431	0.421	0.397	0.398	0.396	0.405	0.048	0.055	0.052	0.055	0.058	0.062
- 1	tox	cc/vc drug 1963 experimental				tox				1	cc/vc	
В	1.578	1.637	0.625	0.664	0.945	1.704				i	1.462	
С	1.360	1.487	0.561	0.583	0.548	1.529				l	1.663	
D	1.233	1.589	0.914	1.025	0.669	1.321					1.681	
E	1.128	0.645	1.256	1.149	1.138	1.186				- [0.742	
F	0.995	0.942	1.036	1.089	1.103	1.031				, [0.879	
G	1.128	0.784	1.121	1.114	1.108	1.127					0.742	
			colorimetric b	ackground								
н	1.151	0.783	0.555	0.453	0.428	0.435						
	tov-cell to	vicity cc-	cell control	Vowvirue con	ntrol	BOLD	- highest dru	o conc		values sho	wn are ontice	Idensities

VIRUS	HIV1	PASSAGE		PROJECT #	
CELLS	CEMSS	PASSAGE		SPONSOR	WALTERREED
SHIPMENT NUMBER	••	OPERATOR KMW		TEST DATE	08/01/00
STRN	RF			DATE READ	08/01/00
REAGENT	0.408	DRUG 1963	25%	50%	95 %
VIRUS CONTROL	0.381	TC (uG/mL)	4.92	21.40	166.00
CELL CONTROL	1.179	IC (uG/mL)	15.40		
DIFFERENTIAL	0.798	ANTIVIRAL INDEX (AI)	0.32		

DRUG	196	3	ANTIVIRAL	TEST VALUES	CYTOTOXICITY	TEST VALUES	
ROW	ON	CONC.	MEAN	% RED. IN	MEAN	% CELL	COLORIMETRIC
PL	ATE	(uG/mL)	O.D.	VIRAL CPE	O.D.	VIABILITY	CONTROL
low	В	0.625	071	0%	1.206	100%	0.027
	C	2	245	0%	1.017	86%	0.020
	D	6.25	0.035	4%	0.824	70%	0.045
	E	20	0.245	31%	0.602	51%	0.147
	F	62.5	088	0%	0.230	20%	0.375
high	G	200	418	0%	024	0%	0.743



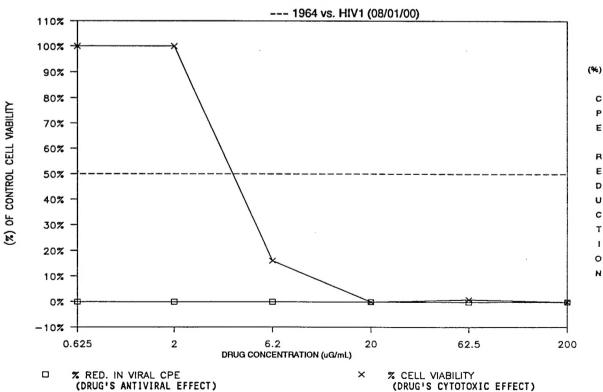
DRUG: --- 1964

TAI: 0.000000 SI: --

	1	2	3	4	5	6	7	8	9	10	11	12
Γ			reagent back	ground					plastic backg	round		
A	0.431	0.421	0.397	0.398	0.396	0.405	0.048	0.055	0.052	0.055	0.058	0.062
Γ		oc/vc					tox	dru	g 1964 exper	mental	cc/vc	tox
В		1.637					1.748	0.786	0.756	0.749	1.462	1.814
C		1.487					1.767	0.696	0.994	0.703	1.663	1.752
D		1.589					0.631	0.424	0.415	0.417	1.681	0.613
E		0.645					0.418	0.408	0.406	0.410	0.742	0.440
F		0.942			1		0.427	0.428	0.431	0.432	0.879	0.468
G		0.784					0.457	0.427	0.433	0.427	0.742	0.437
Γ		-							colorimetric b	ackground		
H							0.455	0.434	0.448	0.439	0.418	0.457
_	tox=cell to	oxicity co-	cell control	ve=virus cor	atrol	BOLD	- highest dru	a conc		volues ebo	wn are ontice	I donniel

					•
VIRUS	HIV1	PASSAGE		PROJECT #	••
CELLS	CEMSS	PASSAGE		SPONSOR	WALTERREED
SHIPMENT NUMBER		OPERATOR KMW		TEST DATE	08/01/00
STRN	RF			DATE READ	08/01/00
REAGENT	0.408	DRUG 1964	25%	50%	95%
VIRUS CONTROL	0.381	TC (uG/mL)	3.26	4.53	15.70
CELL CONTROL	1.179	IC (uG/mL)			
DIFFERENTIAL	0.798	ANTIVIRAL INDEX (AI)			

DRUG	196	4	ANTIVIRAL	TEST VALUES	CYTOTOXICITY	TEST VALUES	
ROW	ON	CONC.	MEAN	% RED. IN	MEAN	% CELL	COLORIMETRIC
PLA	TE	(uG/mL)	O.D.	CPE	O.D.	VIABILITY	CONTROL
low	В	0.625	074	0%	1.324	100%	0.049
	C	2	001	0%	1.342	100%	0.010
	D	6.2	401	0%	0.183	16%	0.031
	E	20	421	0%	019	0%	0.040
	F	62.5	385	0%	0.014	1%	0.026
high	G	200	407	0%	008	0%	0.047



IN VITRO ANTIVIRAL RESULTS XTT ASSAY

TAI: >1.70

DRUG: --- 1965 1.70 SI: ----

	1	2	3	4	5	6	7	8	9	10	11	12
. [reagent back	ground			plastic background					
A	0.421	0.394	0.398	0.400	0.405	0.411	0.056	0.056	0.057	0.056	0.059	0.063
- [tox cc/vc drug 1965 experimental				tox					ec/ve		
В	1.470	1.554	0.801	0.729	0.729	1.600					1.524	
C	1.578	1.567	0.698	0.734	0.638	1.654					1.631	
D	1.535	1.508	0.674	0.693	0.824	1.587					1.574	
E	1.538	0.585	0.692	0.630	0.687	1.668					0.617	
F	1.475	0.612	0.651	0.641	0.637	1.633					0.646	
G	1.054	0.665	0.782	0.924	0.797	1.341					0.676	
i	colorimetric background											
H	0.551	0.460	0.452	0.445	0.425	0.446						
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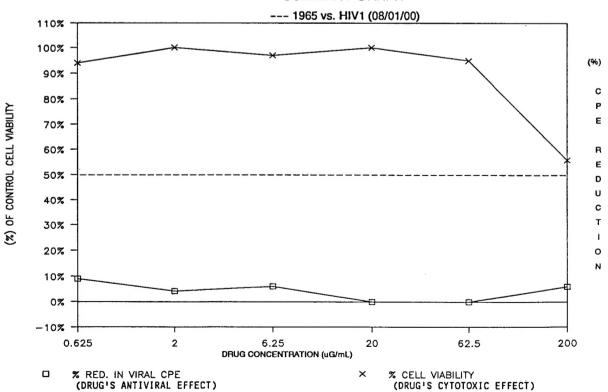
tox=cen toxicity	CC=Con Control	AC-AILDS COULTO

BOLD - highest drug conc

values shown are optical densities

VIRUS	HIV1	PASSAGE		PROJECT #	
CELLS	CEMSS	PASSAGE		SPONSOR	WALTERREED
SHIPMENT NUMBER		OPERATOR KMW		TEST DATE	08/01/00
STRN	RF			DATE READ	08/01/00
REAGENT	0.405	DRUG 1965	25%	50%	95%
VIRUS CONTROL	0.229	TC (uG/mL)	133.00	> 200.00	> 200.00
CELL CONTROL	1.155	IC (uG/mL)			
DIFFERENTIAL	0.926	ANTIVIRAL INDEX (AI)			

DRUG 196	5	ANTIVIRAL	TEST VALUES	CYTOTOXICITY		
ROW ON	CONC.	MEAN	% RED. IN	MEAN	% CELL	COLORIMETRIC
PLATE	(uG/mL)	O.D.	VIRAL CPE	O.D.	VIABILITY	CONTROL
low B	0.625	0.079	9%	1.089	94%	0.041
C	2	0.037	4%	1.191	100%	0.020
D	6.25	0.057	6%	1.116	97%	0.040
E	20	011	0%	1.151	100%	0.047
F	62.5	045	0%	1.094	95%	0.055
high G	200	0.055	6%	0.647	56%	0.146



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